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The Journal of
Obstetrics & Gynaecology
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The Eclamptic Phenomenon and Placental Ischaemia

BY

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IN previous communications evidence was given for the view that eclampsia is preceded by extensive ischaemia of the placenta and that the toxaemia develops only if the lesion is still compatible with a period of foetal survival and with a measure of continuing circulation in the placenta. The evidence was believed to indicate that the toxaemia evolves during the early stages of the placental degeneration and that its degree bears a relation to the mass of the ischaemic lesion (Young,[1] 1914, *et seq.*). This view was based on a series of observations since amplified. (1) After an eclamptic attack ending in immediate foetal death or delivery there was no evidence of this recent massive lesion, whereas, if intra-uterine foetal survival exceeded a period of several days, necrosis (infarction) was found involving more than one-third of the organ and representing, it might be, 10 to 12 ounces or more of placental substance. (2) A progressing toxaemia was generally found to subside rapidly after intra-uterine foetal death or after delivery. (3) In accidental haemorrhage, when the sequence of events could sometimes be traced with considerable accuracy, it was found that, if the placental detachment was immediate and complete, there was

little or no toxaemia; whereas, if detachment was considerable but still compatible with an interval of foetal survival *in utero*, as in concealed accidental haemorrhage, toxaemia was present and often severe. (4) There was evidence that, antecedent to the toxaemia, and responsible for the placental ischaemia, there was an abortion factor. This also expressed itself in the abortions, premature births and stillbirths which commonly terminated the pregnancies of such women. (5) The early abortions of these patients were found to contrast sharply with the late abortions (accidental haemorrhage) for, whereas the former were but rarely, the latter were frequently, associated with toxaemia. Indeed, the pregnancies aborted early were commonly the only non-toxaemic gestations in the whole reproductive history.

In the following pages further evidence will be given in regard to the antecedent nature of the abortion taint and to illustrate how it is conceived to operate in the genesis of toxaemia. Attention has recently (*British Medical Journal*, 22nd March, 1941, p. 445) been directed to those features in which the toxaemic sequence in concealed accidental haemorrhage resembles the clinical state following crush injuries (Bywaters and Beall[2]). The evidence pointing to the possible similarity in the respective mechanisms of these states will be analysed.

Accidental Haemorrhage and Toxaemia

Accidental haemorrhage is associated with late pregnancy toxaemia, pre-eclamptic and eclamptic, in a frequency which is variously stated as from 20 to 80 per cent. There are two main clinical types, the revealed, in which the retroplacental bleeding escapes freely, and the concealed, in which the bleeding, although it may partly escape as a free loss, tends also to accumulate behind the uplifted placenta as a large and increasing blood clot. It is with the concealed type that toxaemia, and especially the severe kinds of toxaemia, are more commonly found.

The relation between accidental haemorrhage and toxaemia has been explained in two different ways. In the first place, it has been generally contended that the retroplacental haemorrhage is the result of the toxaemia. In support of this view there are the other haemorrhagic lesions, e.g. in the liver and brain, commonly found in eclampsia. Further, in many instances, accidental haemorrhage occurs as a terminal phenomenon in

the course of a pre-existing toxaemia. The second view, with which this communication is largely concerned, on the contrary, regards the factor responsible for the placental damage, of which the bleeding is merely one expression, as antecedent and primary, and the toxaemia as a secondary phenomenon.

The Abortion Taint and the Bleeding.

The evidence that the factor responsible for the bleeding antedates the toxaemia comes from two sources. In the first place victims of accidental bleeding with toxaemia in the later months frequently have one or more attacks of bleeding in the earlier months (threatened abortion) without evidence of toxaemia. In the second place, in such women the pregnancies which immediately antedate the pregnancy exhibiting accidental haemorrhage and toxaemia frequently end in abortion or premature birth without any toxaemic manifestations. Such an antecedent pregnancy may, indeed, have ended in accidental haemorrhage without any toxaemic features. Examples of these various possibilities are furnished by the following cases:

CASE 1 (7160). Age 29, 0-para. Had vaginal bleeding for one day at the 4th week of her pregnancy, again slight bleeding at the 8th and 9th weeks, and was in hospital for 14 days with threatened abortion at the 14th week. On all these occasions toxaemia was absent. Thereafter the patient was under supervision at the antenatal clinic and the pregnancy was normal until at the 30th week she had accidental haemorrhage with eclampsia, and a premature stillbirth.

CASE 2 (2084). Age 31, 2-para. First pregnancy ended normally at term. Child 7½ pounds, jaundiced. Died in two-and-a-half days. Second pregnancy ended prematurely at the 30th week; child lived half an hour. Patient's health until next pregnancy, normal. Admitted to hospital at 28th week of third pregnancy with a history of good health till 3 weeks before, when she had slight vaginal bleeding for 4 days. Two days before admission there was a recurrence of bleeding, more severe, ceasing for a day and then coming on profusely. There was not any history of headache, oedema or other evidence of toxaemia. On admission to hospital the pulse was 88, urine albumin free. *Second day*: bleeding still present. Blood-pressure, 118/70. Urine: 34 ounces, no albumin. *Third day*: urine 42 ounces, no albumin. *Fourth day*: slight bleeding with clot. Blood-pressure, 150/85. Jaundice. Urine 45 ounces, albumin, + +. *Fifth day*: delivered of non-macerated stillborn child weighing 2 pounds 3½ ounces. *Seventh day*: Died. The post-mortem revealed typical eclamptic lesions in liver and kidney (Fig. 1).

CASE 3 (19848). Age 24. Had one previous pregnancy in 1937 ending at the 3rd month and without toxaemia. At the 38th week of the 2nd pregnancy in 1938 the patient had accidental haemorrhage with albuminuria and hypertension and the birth of a live child weighing 4 pounds 2 ounces.

These cases exemplify the common finding referred to in previous communications (Young[3]) that there may be inherent in the reproductive history of women who suffer from accidental haemorrhage with toxaemia a taint independent of and separate from toxaemia which tends to interfere with the normal development of their pregnancies (the abortion taint). It is evident in Cases 1 and 2 that if this taint had succeeded in causing abortion in the earlier weeks the toxaemic episode at a later stage of the pregnancy would have been obviated. As we shall see, the influence of foetal survival is found to assert itself throughout our study of the sequence of events underlying toxaemia.

By retracing the reproductive history of toxaemic women we can thus often discover evidence of an antecedent abortion taint. This phenomenon can be studied in the converse way, that is, by taking a series of women, who have never had toxaemia but who exhibit the abortion taint, and noting the fate of their subsequent pregnancies. The result of such a study is shown in Table I. It relates to women who "booked" for their confinement and in whom the immediately antecedent pregnancies had ended in abortion, premature birth or stillbirth. Those in whom there was evidence or suspicion of previous toxaemia were excluded. This left a consecutive series of 142 women.

TABLE I.

Fate of Immediately Succeeding Pregnancy after Abortion, Premature Birth or Stillbirth without Toxaemia.

Total subsequent pregnancies			142
Abnormal		65 (45.8 per cent)	
Toxaemia	25 (17.6 per cent)		
Abortion, premature birth or stillbirth without toxaemia	16		
Live birth at term without toxaemia, but one or more attacks of bleeding during pregnancy	24		
Normal		77 (54.2 per cent)	

Thus, out of 142 pregnancies following immediately upon a gestation which ended in abortion, premature birth or stillbirth only 77, or 54.2 per cent, terminated normally, while 25, or 17.6 per cent, exhibited toxaemia. In a control series of 106 women whose immediately preceding pregnancy had ended normally the results are shown in Table II.

TABLE II.

Fate of Immediately Succeeding Pregnancy after Normal Full-time Pregnancy

Total subsequent pregnancies			106
Abnormal	9	(8.5 per cent)	
Toxaemia	2	(1.8 per cent)	
Abortion, premature birth or stillbirth without toxaemia	3		
Live birth at term without toxaemia, but one or more attacks of bleeding during pregnancy	4		
Normal	97	(91.5 per cent)	

For the analysis of the two sets of records toxaemia is defined as albuminuria with or without hypertension, oedema, etc. In 17 cases out of a total of 142 cases analysed in Table I, there was a continued or repeated blood-pressure of 140 mm. Hg. systolic or over, and 90 mm. Hg. diastolic or over without other evidence of abnormality, such as oedema. In Table II there were 7 such cases in the total of 106. In neither table are such cases included under the category of toxaemia. For reasons which will be considered later (p. 242) it is becoming increasingly clear that hypertension is an unsound basis for the classification of true or specific toxaemia. It is to be noted that the records do not express the full measure of the taint because the majority of the women came to the clinic when the major risks of abortion had passed (second to fourth month).

This study of the reproductive history from two different angles, retrospective and prospective, we regard as indicating that the abortion taint when intrinsic in the constitution of toxaemic women is antecedent to the toxaemia. At the same time this taint is often so closely associated in its timing with the toxaemic outbreak, as, for example, in accidental haemorrhage, as to suggest that it may play a part in the genesis of the toxaemia (Cases 1 and 3).

Before proceeding further we would remind the reader of the different roles of the foetus and placenta in the pathogenesis of the pre-eclamptic and eclamptic process so far as these seem to be well established. It is known that the process can occur in hydatid mole and that, therefore, the foetus is not essential. Further, while pathology of a definite type (massive necrosis or infarction) is common in the placenta, no special pathology is identified with the foetus. Indeed, the fact that the foetus can often survive both *in* and *ex utero* the most virulent eclamptic

attack which kills the mother, and the finding that, in accidental haemorrhage, this survival is conditioned by the degree in which the placental detachment involves the circulation of the placenta, indicate that the common foetal death is determined, not by a direct assault on the foetus, but by some influence which compromises the placenta. At the same time, as we have seen in Cases 1 and 2, foetal survival is necessary for the inception and development of the toxaemia; in these cases if the foetus had died several weeks or even several days earlier, there would not have been any toxaemia. On the one hand, the continuing survival of the foetus during the earlier days was possible only because the placental mass involved was below the threshold of danger to the child and, on the other hand, the ultimate death of the child, by which time the toxaemia had gathered volume, occurred only when the placental mass affected had increased above this threshold. These findings are in keeping with the well-known observation that at the climax of the toxaemia foetal death *in utero* (or delivery) may lead to a sudden subsidence of the attack. They also lend an added significance to the fact that the aborted pregnancies in such women may be the only ones free from toxaemia. For it is clear that death of the foetus and abortion imply a process involving only a small total placental mass.

It has been shown in previous communications (Young[1]) that the study of the placenta may provide evidence by which we can assess (*a*) the extent to which it has been involved, and (*b*) with approximate accuracy the time which has elapsed between the first attack on the placenta and the death (or delivery) of the foetus (see also Cases 6 and 8 to 11). In the production of the infarct two changes are noticed, firstly, a stasis and coagulation of the blood in the intervillous spaces, and, secondly, and probably as a sequence, a collapse of the corresponding area with a crowding of the villi into a solid mass (Young[1]). In its most recent or acute phase the infarct is difficult to detect, but after it has existed for a short interval (probably within 24 to 48 hours) its solid consistence and purple colour can both be brought into evidence if the cut section is washed in water which quickly extracts the fresh blood from the surrounding healthy placenta. In concealed accidental haemorrhage the adherent clot may indicate accurately the extent of separation, especially where the pressure of the clot in the uterus has caused a saucer-shaped cup in the placenta. The degree to which the infarction process has evolved in the

subtending placenta corresponds to the age of the separation. Over a recently formed clot the placenta may appear normal both to the naked eye and to the microscope (Young[1]). In the later stages the infarct becomes chocolate-coloured and then after several weeks passes through changes ending in the characteristic old white infarct. Further, infarcts frequently depict the history of this process exhibiting, for example, in the smaller infarcts of differing age the repeated slighter assaults on the placenta in the earlier months, and in the massive infarcts of recent formation portraying the crescendo of damage ending in foetal death. The relation between placental infarction and foetal death is well established. It may, indeed, be regarded as a common expression of the abortion taint, and it follows that when this is antecedent to the toxaemia the infarct must share in this priority. It is known that, while infarction is more evident in toxaemic cases, it can occur in the absence of toxaemia and this has furnished an argument for those who deny it any significance in the aetiology of toxaemia.

Bartholomew and Colvin,[4] while supporting my views in regard to the primary place of placental infarction in toxaemia, believe that this infarction is due to interference with the foetal circulation as the result of endarteritis of the vessels of the chorion and foetal villi. This view, as I have elsewhere pointed out (Young[1]), is opposed to certain well-established facts in physiology and pathology which prove that the chorionic epithelium can live and proliferate in the absence of the foetal circulation so long as the maternal blood supply is maintained. Thus, the trophoblast proliferates actively during its earliest phase before the foetal vessels are developed, while in hydatid mole and chorionepithelioma there is a similar active growth in the absence of a foetal circulation. The same appearances are sometimes found in the case of retained fragments of placenta which preserve their attachment to the uterine wall and in the case of chorionic villi in tubal pregnancy which may remain alive at their tips in some places where the maternal circulation is maintained after the main villous trunks have undergone fibrinous necrosis. We often find an interesting appearance which in a sort of obverse manner conveys the same lesson. In the centre of an infarct in which the smaller villi are completely necrotic we may find imbedded a villous trunk in which the red blood cells are well preserved, thus suggesting that the circulation in the larger villous branches may actually persist after the terminal branches are completely infarcted.

The Bleeding—Toxaemia Sequence.

In our latest series of 79 consecutive cases of accidental haemorrhage albuminuric toxaemia was present in 20 or 25.3 per cent. In such patients the toxaemic manifestations frequently antedate the bleeding episode, and this has commonly led clinicians to regard the retroplacental bleeding as a result of the toxaemic process. The present writer and others (Essen-möller,[5] Whitridge Williams[6]) have pointed to the difficulty of accommodating the known facts within such a conception.

(1) A considerable proportion of cases (74.7 per cent in this series) do not present any evidence of toxaemia. That this division into two clinical types does not imply a dual aetiology is shown by the fact that in both types the accidental haemorrhage in the later phase of pregnancy may be the culmination of an abortion taint which in an earlier phase expresses itself without any evidence of toxaemia. Cases 1 and 2 are examples of this common finding in toxaemic cases.

(2) Accidental haemorrhage may develop in two consecutive pregnancies in the same patient with toxaemia in one and no toxaemia in the other (Young[3]).

(3) Concealed accidental haemorrhage is associated with a much higher incidence and a graver form of toxaemia than the revealed type. Thus in our 79 patients albuminuric toxaemia was present in 20 (25.3 per cent), the differential distribution being: revealed, 7 in 59, or 11.8 per cent; concealed, 13 in 20, or 65.0 per cent. All the grave cases were included in the concealed group. These findings conform to those of other observers and they indicate the close correlation between concealment and toxaemia. This striking correlation is not easily explained on any view which ascribes the bleeding to the toxaemia, for such a view implies that the tendency to concealment is determined by the severity of the toxaemia. This is not supported by the facts. The distinguishing feature of a concealed case is the retention of the placenta for an interval after the onset of the process with a gradually increasing involvement of its circulation leading in many cases to foetal death. That this placental retention is not dependent upon toxaemia is indicated by the finding that concealment and its associated high foetal death-rate are found frequently in non-toxaemic cases. Thus out of the total of 20 concealed cases in our series as high a proportion as 7 (35 per cent) did not have any toxaemia. There are similar findings in respect of the foetal mortality. The foetal mortality in a total of 20 concealed cases was 16, or 80 per cent,

as compared with 6 in 59 revealed cases, or 10.2 per cent. But in 7 concealed cases in which toxaemia was absent there were 4 foetal deaths (57.1 per cent).

A consideration of the unique lesion known under the term "utero-placental apoplexy" provides even more striking testimony against the view that accidental haemorrhage is caused by toxaemia. Here, in association with a large retroplacental haematoma, there is a wholesale ploughing up of the uterine muscle and sometimes of the tissues of the broad ligaments, Fallopian tubes and ovaries, with extravasated blood. In the extreme form the uterus and its appendages have an appearance suggesting acute strangulation. This unique and remarkable condition is apt to be associated with an extremely grave form of toxaemia, but against this being regarded as the causal factor is the fact that the complete picture may be exhibited in the total absence of toxaemia. Whitridge Williams,[6] in a series of 10 cases, did not find any toxaemia in 5, and we have found the condition at Caesarean section in 2 non-toxaemic cases.

The above considerations would seem to justify the conclusion that accidental haemorrhage is not to be regarded as a result of toxaemia. The total evidence is in keeping with the view that the placental lesion is a manifestation of an antecedent abortion taint and that in certain circumstances this lesion may be associated with or followed by toxaemia. The striking correlation between concealed accidental haemorrhage and the grave form of toxaemia suggests that the severity of the toxaemia is determined by the extent of the placental involvement.

(4) The strongest argument against the toxaemic origin of accidental haemorrhage is derived from a study of those cases in which the haemorrhage develops in a woman who has not shown any previous evidence of toxaemia. In many such cases a careful study of the clinical sequence demonstrates that the toxaemic phenomena appear after the onset of the retroplacental haemorrhage (Case 2).

ALBUMINURIA DEVELOPING AFTER ACCIDENTAL HAEMORRHAGE

CASE 4 (13514). July 6th. At her routine visit to the antenatal clinic at 37th week of pregnancy, the latter was found to be normal. Urine: albumin nil. July 8th, 6 p.m. Severe lower abdominal pain. 8.30 p.m. Admitted to hospital. Diagnosis: concealed accidental haemorrhage. Urine: albumin nil. 12 midnight. Urine: albumin 700 mgm. per 100 c.c. No blood transfusion.

CASE 5 (13659). July 16th, 11 a.m. Routine visit to antenatal clinic

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when 39 weeks pregnant. Urine: albumin nil. Complained of lower abdominal pain. Uterus tender. Patient advised to come into hospital. Decided to go home first. At home pain became very severe and she took a taxi to hospital. 2.30 p.m. Diagnosis: concealed haemorrhage. 5.45 p.m. Urine withdrawn by catheter: 2 ounces, albumin 1600 mgm. per 100 c.c. No blood transfusion.

Case 6 (13896). Age 37, para-3 + 1 abortion. The 3 first pregnancies were associated with hypertension and ended at term with living children. The last pregnancy ended at 16 weeks. Admitted on 11th May, 1941, at the 32nd week of her 5th pregnancy after an attack of abdominal pain followed by moderate blood loss. No oedema, headache or other evidence of toxaemia. Blood-pressure 130/80. Kept in bed and bleeding ceased. Remained well until May 28th, 1941, when the following sequence was observed.

28th May, 1941, 10 a.m. Well. Blood-pressure, 105/75. Urine: albumin free. 12 noon. Abdominal pain followed by vaginal bleeding. 12.40 p.m. Blood-pressure, 160/90. Urine: albumin free. 1.30 p.m. Caesarean section carried out with delivery of living infant weighing 4 pounds 12 ounces. 6.30 p.m. Blood-pressure, 148/88. Urine: no albumin. 29th May, 1941, 10 a.m. Blood-pressure, 150/82. Urine: albumin 200 mgm. per 100 c.c. Thereafter the blood-pressure remained raised for 10 days and the albuminurea lessened gradually, disappearing after 18 days. There was not any drop in the urinary output or rise in the blood urea. *Placenta*: Small infarct indicating previous damage and probably dating from bleeding episode 18 days before. Decidual clot covering less than one third of organ in which infarction process is not recognizable (Fig. 2).

In severe cases suppression of urine is a striking feature. In many this is found to develop after the onset of the bleeding. The following is an example.

Suppression of Urine Developing after Accidental Haemorrhage

Case 7 (4080). 15th December, 12.10 p.m. Sudden severe abdominal pain. Diagnosis: concealed accidental haemorrhage. Up to this point she had passed urine normally and at 1.30 p.m. 2 ounces were removed by catheter. Thereafter there was complete suppression for 33 hours. 16th December, 1 a.m. Blood transfusion, 500 c.c. 10.30 p.m. Urine: 6 drachms, blood-stained. Suppression established before blood transfusion. (See also Case 8.)

Azotaemia Developing After Accidental Haemorrhage.

In the majority of cases the toxaemia associated with accidental haemorrhage conforms to the ordinary classical pre-eclamptic type. In the graver forms, associated especially with concealed cases, the condition may, as many writers have shown, mature into the full eclamptic picture; there is one such case in our series of 13 toxaemias in the concealed group. It

is, however, well known that cases of accidental haemorrhage, especially if concealed, are apt to develop evidence of renal failure, in this way differing profoundly from the typical pre-eclamptic and eclamptic phenomenon. In 5 of our 13 cases of concealed accidental haemorrhage with toxaemia there was a significant rise in the blood urea, and in 4 this was marked. These patients exhibited the features described by previous writers: severe abdominal pain and shock (betokening the rapidly developing retroplacental bleeding with, in some instances, extensive bleeding in the uterine musculature), continuing suppression of urine or oliguria with blood-stained urine containing renal casts and leucocytes, and a rapidly rising blood urea. Marked albuminuria is also present. The findings are represented graphically in Fig. 3. It is seen that in 3 cases we can date the origin of the rising curve of blood urea, and in all it is clear that *the azotaemia develops subsequent to the intra-uterine crisis*. As previous writers have shown, this azotaemia is an expression of a defective concentrating function in the kidneys (Gibberd[7]). The findings are in keeping with the view that the renal failure is sequential to the placental lesion. They are not easy to reconcile with the view that the renal lesion is an expression of a toxaemic state antecedent to the retroplacental bleeding.

We shall now consider in further detail selected cases in which a study of the sequence furnishes evidence in support of the view that the toxaemic phenomena are sequential to the utero-placental damage.

Case 8 (5369). Age 37, 5-para. Four full-time normal pregnancies. One (the second) ended in stillbirth at 28th week. Admitted 27th January, 1936, at 28th week of 6th pregnancy. Stout pale woman who stated that before the onset of the present symptoms the pregnancy had progressed normally. No oedema or headache. No antenatal care. When out shopping and feeling well at 11 a.m. on 27th January, 1936, had acute generalized abdominal pain. Went to bed and an hour later, on trying to get up, fainted and vomited soon after. Since then she had fainted three times. Headache and slight blurring of vision for 4 days previously. Urine: in amount about half an ordinary tea-cup passed at 7 a.m., none since. On admission at 5 p.m. on 27th January, 1936, pulse-rate, 110; respiration-rate, 24; blood-pressure, 155/105. Uterus corresponded in size to 34 weeks and was tender over the fundus and left side. Foetal mass not felt, and no foetal heart heard. Foetal heart heard by private doctor at 1.53 p.m. No vaginal loss. Urine: only 3 c.c. withdrawn by catheter, boiled almost solid. Diagnosis: concealed accidental haemorrhage with severe toxaemia. 7 p.m., lost 8 to 10 ounces of blood. 10 p.m. Losing continuously. 28th January, 1936. Bleed-

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ing, pulse-rate, 104; blood-pressure, 110/90. Pains every 10 minutes. No secretion of urine. 12.45 a.m. Delivered foetus and placenta, i.e., about 14 hours after onset of acute symptoms. Foetus 26 weeks approximately, and freshly dead, no maceration and no discoloration of umbilical cord. About three-quarters pint of old black clot adherent to placenta. Also passed other old and fresh blood totalling with adherent clot ± 2 pints. Blood-pressure, 100/60. Moderate shock. Glucosaline (5 per cent) administered rectally and intravenously. 30th January, 1936. Haemoglobin 26 per cent. Blood-transfusion, 1250 c.c. The suppression of urine continued for 4 days. By the 5th day the blood urea reached its maximum of 360 mgm. per 100 c.c. Thereafter the recovery was slow but continuous. *Placenta*: Extensive recent retroplacental haemorrhage with subtending area of recent infarction involving about one-third of the organ. This area varied in age, the larger part being fresh (about ?48 hours old). Other areas of infarction were less recent and were estimated as being at least 7 to 10 days old, one or two being of several weeks' duration.

The data in this case are represented in an approximate manner in Fig. 4. We can be reasonably certain that the onset of the placental damage preceded the onset of the toxaemia, and completely certain that the massive visible involvement of the placenta, reaching finally one-third at least of the organ, was rendered possible only by the survival of the foetus, which lived till a short time before delivery. The area of recent and adherent blood clot is consistent with an involvement of one-half or more of the placenta before foetal death. The clinical sequence seen in this case is usually associated with the concealed type of accidental haemorrhage. This association is to be explained by the fact that the concealment or retention of the placenta within the uterus after the onset of the morbid process allows of the evolution of the sequence of changes, that is, the gradual and ultimately massive occlusion of the placental circulation, before the death of the foetus brings it to a complete and abrupt termination. It is to be noted that the urinary suppression developed subsequent to the intra-uterine crisis and was established before the development of shock and before the blood transfusion.

Case 9 (7160). This case is also quoted under Case 1. Age 29, 0-para. Last menstrual period, 10th December, 1936. Expected date of delivery 17th September, 1937. Threatened abortion at 8th, 9th, and 14th weeks. On the last occasion was in hospital for 2 weeks. First attended antenatal clinic at 19th week when blood-pressure was 120/80. Attended periodically until 22nd June, 1937, and during this time the blood-pressure ranged between 110 and 120 systolic and 76 and 86 diastolic. At no time was there albuminuria or other evidence of toxaemia. On 29th June, 1937, i.e., 7 days

after the last antenatal visit and at the 29th week, the patient was admitted to hospital. The history was that she remained well till 2 days before (27th June, 1937) when swelling of legs was noticed. On the day before admission (28th June, 1937) her face began to swell. On the night before admission she had severe headache and blurring of vision. At 9 a.m. on the day of admission she had a profuse vaginal bleeding. 11 a.m., admitted. The patient was pale, pulse-rate 100, blood-pressure 160/86, eyes and face oedematous, clothes saturated with blood, but active bleeding not present. Two ounces of blood-stained urine were obtained by catheter: albumin 1000 mgm. per 100 c.c. which contained blood and granular and hyaline casts (next day). At 3.30 p.m. Caesarean section was carried out with delivery of fresh (non-macerated) child, weighing 2 pounds 12 ounces. Blood transfusion, 900 c.c. Half an hour after delivery the patient had eclamptic fit and, within 2½ hours, three more. 5th July, 1937 (7th day). Blood urea 186 mgm. per 100 c.c. *Placenta*: Small area of infarction estimated as several weeks old: a larger area of more recent date, while a considerable part (about one-half of the organ) was covered by adherent decidual clot and, though congested, did not show evidence of infarction.

The clinical sequence is represented diagrammatically in Fig. 5. The abortion taint antedated the toxaemia; it was in operation at the 8th, 9th, and 14th weeks, and, as judged by the age of the placental changes found after delivery, it again struck at this organ some considerable time before the first evidence of toxaemia. It struck again at a later date and the placental damage now increased rapidly, being accompanied by haemorrhage and detachment. The increasing and ultimately massive placental involvement was followed by the onset of toxaemia which, increasing rapidly, reached its zenith within 2 days. The foetus was fresh, and must, therefore, have survived till a short time before delivery.

Case 10 (13615). Age 29, 6-para. Previous pregnancies all normal. Attended antenatal clinic from the 24th week of her 7th pregnancy until the 35th week (24th April, 1941). Blood-pressure varied between 110 and 120 systolic and 70 and 80 diastolic, the urine was albumin free and there was not any evidence of toxaemia. On 29th April, 1941, i.e., 5 days after the last visit to the clinic, she was admitted to hospital with vaginal bleeding. No headache, sickness or oedema. At 1 a.m. she had severe backache and a desire to defaecate. The bowels were opened and she returned to bed. She felt the child move at this time. Noticed she was losing blood. At 4.45 a.m. was admitted to hospital. Pulse-rate 80, blood-pressure 120/60. Urine: albumin 400 mgm. per 100 c.c. Foetal heart not heard. Diagnosis: concealed accidental haemorrhage. 6.30 a.m. in labour. Pulse-rate 150, suggesting severe intra-uterine bleeding. The membranes were ruptured artificially, and at 7 a.m. she gave birth to a stillborn freshly dead foetus weighing 5

pounds 15 ounces. The delivery of the placenta was followed by two large clots. Blood-pressure, 80/50; pulse-rate 128; a transfusion of 600 c.c. stored blood. Throughout there was no obvious diminution in the urinary output. *Placenta*: did not show any naked-eye morbid change except one small intra-placental haemorrhage. There were no definite microscopical changes except some coagulation in the intervillous spaces.

The sequence is represented in Fig. 6. We cannot tell exactly when the retroplacental bleeding and placental detachment began, but from an examination of the placenta, and from the fact that the foetus was living to near the end, we can tell with certainty that the onset of the detachment could not have antedated the onset of the symptoms by more than 24 to 48 hours, and the interval was possibly much less. We are thus dealing with a sequence which both in regard to placenta and to toxaemia is greatly reduced in tone and emphasis as compared with that in Cases 8 and 9. The sudden maximal involvement of the placenta and speedy foetal death are associated with a minor degree of toxaemia. There was no oliguria or raised blood-pressure, the albuminuria was moderate and the maximal blood urea 75 mgm. per 100 c.c. This is an example of a common type of case. Many further examples could be cited in which with immediate foetal death or delivery there is no toxaemia.

Eclampsia and Pre-Eclampsia

In accidental haemorrhage the bleeding episode furnishes a time point around which we can sometimes build up with approximate accuracy the chronology of events ending in toxaemia; we then discover that the toxaemia succeeds the haemorrhage and the placental damage. In the ordinary pre-eclamptic and eclamptic sequence there is not usually a convenient starting point of this nature. Nevertheless the following considerations suggest that the factors underlying eclampsia may be similar to those operating in the toxaemia of accidental haemorrhage. (1) The latter generally is frankly pre-eclamptic or eclamptic (Cases 6 and 9), the uraemic sequence being rare. (2) Accidental haemorrhage with its acute toxaemic accompaniment, sometimes eclamptic in nature, may be the terminal phase of a pre-existing pre-eclampsia. (3) The antecedent nature of the abortion taint is frequently apparent in pre-eclamptic and eclamptic toxaemia (Young[3] and Cases 2, 6 and 9 and Table I). (4) In eclampsia, as in severe toxaemia of accidental haemorrhage, when a sufficient interval intervenes before

foetal death or delivery, a recent and massive placental lesion is recognizable (Young,[1] and Case 9). As we have indicated on a previous page and as has been shown elsewhere (Young[1], Fordyce and Johnstone[8]) the area of the placenta involved may be as great as one-third to one-half of the organ. The following recent case exhibits this correlation.

CASE 11 (15553). Age 21, 0-para. Between the 22nd and 26th weeks, while under supervision at the antenatal clinic the pregnancy progressed normally. Admitted to hospital at the 26th week with 5 hours' history of severe epigastric pain, diarrhoea and vomiting. On admission there was slight oedema of the left leg. Blood-pressure, 150/89. Urine 200 mgm. albumin per 100 c.c. Not in labour. Treated with sedatives and the condition improved for 2 days. Four days after admission the blood-pressure rose to 170/88 and the patient had a typical eclamptic seizure lasting 2 minutes and followed by 10 minutes' coma. The condition improved rapidly, and the patient refused to consider the termination of pregnancy. The patient was delivered 3 weeks later of a 34 weeks' infant, weighing 3 pounds 9 ounces, who survived. *Placenta*: about one half of the organ was the seat of infarction estimated to be 3 weeks old.

Cause of the Toxaemia.

We believe that from the preceding evidence we can draw three conclusions. (1) The toxaemia follows the placental damage. (2) There is a close correspondence between the degree of the toxaemia, on the one hand, and the extent of placental involvement and the duration of the circulation in the placenta, on the other hand. (3) The findings are in keeping with the view that the damaged placenta furnishes the factor responsible for the later stages of the pre-eclamptic and eclamptic sequence. In the present state of our knowledge we can only speculate on the exact nature of this influence. Much experiment has failed to reveal conclusively the existence of toxic matter in the placenta or blood of toxaemic cases and attempts by autolysis and other means to isolate from the normal placenta such a toxic agent, though sometimes suggestive, have failed to carry conviction (Young[1]).

A relatively large proportion of concealed cases of accidental haemorrhage, as we have seen, have superimposed upon the pre-eclamptic and eclamptic toxaemia additional features in the form of shock and renal failure; in our 20 concealed cases 5 out of 13 toxaemias are of this nature. It is known that these grave cases are apt to exhibit a distinctive haemorrhagic and sometimes necrotic lesion in the uterine musculature. There

would seem to be no reason to doubt that this lesion owes its origin to the same factors as those responsible for the massive decidual bleeding and that it is, therefore, antecedent to the toxaemia. That it is not a result is indicated by its occurrence in non-toxaemic cases. This lesion may contribute to the production of the shock typically present, which is sometimes out of all proportion to the retroplacental blood loss (see Whitridge Williams[6]). It is also a matter for consideration how far this muscular lesion may contribute to the causation of the renal failure. It is true that this failure, with impairment of the concentrating function (Gibberd[7]) and a raised blood urea, has been attributed to the circulatory collapse following shock from haemorrhage or other cause, or from blood transfusion. But, as we have seen, there may be indisputable evidence in the clinical records (Cases 4, 5, 7, 8, and 9) to exclude the operation of shock or of transfusion or of both in, at least, the initiation of the renal lesion. Further, in this initial stage, the expression of the lesion (severe albuminuria, with anuria or oliguria) is similar to that in the ordinary eclamptic sequence in which shock plays little or no part. There is, also, the evidence of every large obstetric service in which blood transfusion is a frequent procedure for the shock associated with blood loss in such relatively common emergencies as placenta praevia, 3rd stage and post-partum haemorrhage. Thus, in a total of over 9,000 pregnancies, apart from one fatal case of pyelonephritis, we have found renal deficiency with a significant rise in blood urea restricted to two categories: (1) Cases of concealed accidental haemorrhage; it occurred in 5 out of a total of 20 and (2) after difficult labour, 4 cases. This second group is at present the object of special study.

Analogy with the Crush Syndrome.

In a previous communication[9] attention was drawn to the analogy between the placental hypothesis of pregnancy toxaemia which we have advanced, and the view of Delbet,[10] Quenu[11] and others who attributed the toxaemia following severe wounds to absorption of toxic products from the damaged tissues. The demonstration by Delbet that the products of muscle are toxic in the earliest stages of disintegration supported this analogy. This parallelism has been reinforced by the recent investigations of Bywaters and Beall[12], and others on the syndrome found in crush injuries. On its clinical side—the initial shock of variable intensity, the rapidly developing renal lesion with suppression

or oliguria and a blood-stained urine containing granular, hyaline and other forms of casts, a rapidly rising blood urea, oedema and sometimes hypertension—the crush syndrome closely simulates the syndrome of concealed accidental haemorrhage. The chief morbid anatomy is found in the kidneys in the shape of tubular degeneration and of haematogenous casts in the tubules which Bywaters and Delory[13] have identified as myohaemoglobin. The renal picture which has been specially identified with fatal toxaemic cases of concealed accidental haemorrhage with anuria is that of symmetrical cortical necrosis. Parkes Weber[14] believed that the primary process was a destruction of the tubular epithelium and that the thrombosis, which constitutes a striking feature in most cases, was secondary. More recently the tendency has been to regard the thrombosis as primary (Glynn and Briggs,[15] Jardine and Kennedy,[16] Kellar and Arnott[17]), although Dunn and Montgomery[18] have suggested that the initial process consists of a complete stasis of the glomerular circulation to which both the thrombosis in the afferent and the intralobular vessels and the tubular degeneration are secondary. Shaw Dunn and Montgomery have shown that in most cases the glomeruli exhibit the endothelial swelling and the swelling and fibrillation of the capillary basement membrane found in pre-eclampsia and eclampsia.

Bratton[19] has recently described the renal lesions found in 6 fatal puerperal cases of antepartum bleeding associated with anuria or oliguria. In none had blood transfusion been given. There was tubular degeneration, with haematogenous casts in 5, and a picture like that found in the crush syndrome; Bratton's paper includes a description of the similar lesion in an air-raid casualty. Through the courtesy of Dr. Bratton and the medical superintendents of the hospitals concerned I have had the opportunity of studying the records of 5 of the cases. In 3 with complete anuria and the full renal picture the clinical evidence suggested that the patients had suffered from accidental haemorrhage at about the 26th to the 28th weeks of pregnancy. In one of these, as Bratton indicates in his paper, a haemorrhagic and necrotic lesion was found in the liver. In one of the remaining 2 cases the patient suffered from concealed accidental haemorrhage and eclampsia at the 30th week of pregnancy. So far as we can discover the lesion described by Bratton has not before been identified with the toxaemia of accidental haemorrhage, although Fahr,[20] and Baird and Dunn[21] have previously noted haematogenous casts in the kidney of eclampsia.

The relation between this lesion and symmetrical cortical necrosis is a subject for further study. Meanwhile it is interesting to note that a case of renal cortical necrosis following severe crush injuries has been recorded (McFarlane[22]).

The available evidence thus suggests a basic similarity, both clinical and pathological, between the obstetrical and surgical toxaemias. The tubular lesion naturally raises the question of damage by a toxic agent in the process of excretion and the remarkable renal localization characterizing both the crush and the accidental haemorrhage syndromes, may, as Shaw Dunn, Gillespie and Niven[23] suggest in discussing the crush phenomenon, be an expression and result of the concentrating function of the tubules at an early stage when this function is active. In the obstetric condition the eclamptic accompaniment complicates the issues and this may, to some extent, explain the varying and confusing renal picture. At the same time it is important to recognize that tubular failure is rarely present in the eclamptic phenomenon. When this exists it may imply a superimposed toxic agent of extra-placental origin.

The Aetiology of the Abortion Phenomenon

The study of the influences responsible for the abortion taint at the back of the toxaemic phenomenon necessarily involves the survey of a wide territory. In this place any detailed scrutiny of the subject is impossible, and only some general and tentative observations will be made. At the same time, there are some considerations which at the outset may help us to narrow the field. One of the most common factors in abortion is a gross developmental abnormality in the foetus. As Moll and others have shown, a high proportion of foetûs aborted early exhibit such abnormalities, and it is likewise known that prematurity and stillbirth are not infrequently associated with spina bifida and anencephaly. There is no clear evidence that vitiation of pregnancy from such factors plays any important part in the abortion-toxaemia taint. At the same time in the absence of fuller knowledge it would be unwise to foreclose on such a possibility, especially as the systematic and environmental factors responsible for abortion may express themselves in different ways. As an example, we may cite the claims made by some observers that dietetic deficiencies which ordinarily provoke abortion in animals may be accompanied by a high incidence of abnormality in the litter.

Another consideration which still further defines the ground to be explored is that the abortion taint responsible for toxaemia is frequently recurrent in the sense that it is apt to reappear in successive pregnancies (Young[3] and Table I). For this reason the investigations which have recently indicated the existence of a defective hormonal mechanism, especially in respect of progesterone, in habitual abortion (Browne, Henry and Venning[24], MacGregor and Stewart[25]) have a possible bearing on our problem. These investigations are in accord with the established *rôle* of the corpus luteum in the maintenance of early pregnancy and they have rationalized previous clinical success with progesterone in the treatment of habitual abortion and stillbirth.* These observations have an added significance in view of the growing evidence that the toxaemic state may have an endocrinological basis. Thus Vorzimer, Fishberg, Langrock, and Rappaport[26] have, from a study of 120 toxaemic patients, given evidence that "toxaemia is an endocrine disturbance evolving in women with a pre-existing constitutional abnormality of the endocrine glands." These authors found that the average pre-pregnancy weight of patients who developed toxaemia was 21.8 pounds more than that of the normal controls. The incidence of obesity was high. The average weight/height ratio of the toxaemia series was 2.5 as contrasted with a ratio of 2.08 in the controls. Of women with toxaemia 55 per cent had changes in the facies of the "acromegaloid" type as contrasted with 5 per cent in the controls. In 98 per cent of the patients with toxaemia there were one or more of these and other endocrine stigmas, and in a large majority there were 2 or more. Only 15 per cent of the normal controls presented any endocrine stigmas, and only 3 per cent had more than one stigma. Further, Smith and Smith[27] have claimed to find a rise in serum prolan, a fall in pregnandiol excretion and a low oestrin value in serum and urine in cases of toxaemia. These changes appear several weeks before the clinical signs, and they also are

* Hain, A. M. (*Journ. Endocrin.*, 3, 1, 10) has recently reported normal gonadotrophin and pregnandiol outputs in 60 per cent of women with threatened abortion, and cites cases of abortion in which, with a normal pregnandiol output, there was an increased oestrogen level. She believes that there is little doubt that the combined secretion of oestrogen and progesterone is essential for the maintenance of pregnancy but that morbid changes may be an expression not of deficient production but of defective utilization.

present in patients in whom pregnancy eventually terminates prematurely without toxaemic manifestations.

The study of pregnancy in association with diabetes furnishes evidence pointing to the possible significance of an endocrinological factor in the common abortion-toxaemia complex found in this condition. It is notorious that, despite the marked improvement in the maternal prognosis since the introduction of insulin, there has been little alleviation in the risk to the foetus. Thus Joslin[28] gives a pre-insulin foetal death-rate of 44 per cent, and a post-insulin rate of 38 per cent (the latter figure excluding therapeutic abortion). This high foetal death-rate is associated with a persistently high toxaemia rate (Joslin 45.7 per cent). The investigations of White, Titus, Joslin, and Hunt[29] give strong evidence that disturbance of the sex hormones is responsible for both the high foetal death-rate and the toxaemia. In 35 pregnant diabetics they found that "of 14 whose values for serum prolan were normal, none developed pre-eclamptic toxaemia, none miscarried, and there was one foetal fatality. Out of 10 patients whose values were hypernormal and who received no therapy, 7 developed toxaemia, 3 miscarried, and there were 6 foetal fatalities; out of 9 treated cases (massive oestrin and progesterone therapy), 8 had toxaemia which subsided, none miscarried, and there was one needless foetal death, the case in which therapy was omitted." It is clear that diabetes provides a rich field for the study of the factors responsible for the abortion-toxaemia phenomena. Of special interest in this connexion is the evidence which suggests that the anterior pituitary is concerned with the genesis of diabetes (Young[30]). A further possible correlation between diabetes and toxaemia is the high incidence of hypertension found in the former state.

The morbid anatomy of the uterine changes in abortion has received little study, and there is from this source scant information as to how the systemic abortion factors operate on the uterine tissues. Certain facts, however, as studied in fresh material are reasonably clear. One of the most important changes is a dilatation, often extreme, of the vessels throughout the entire decidua. There is widespread extravasation (Fig. 7), and thrombosis and necrosis are common even in early material, but their significance is uncertain. The vascular phenomena in their nature and extent resemble those found in the late premenstrual and early menstrual phases and in the dysfunctional bleedings, which are known to be an expression of quantitative changes in hormonal levels. There is thus much reason in

analogy for postulating a similar mechanism in the bleeding and the separation of abortion.

In a previous communication (Young[1]) a similar phenomenon was described in accidental haemorrhage, namely a vascular engorgement with haemorrhage affecting the decidua widely (Fig. 8). The decidual haemorrhage behind the placenta is merely an excessive manifestation of a widespread process which, if also affecting the muscular wall, results in the condition of "utero-placental apoplexy."

The exact nature of the vascular changes in those cases in which the abortion taint causes ordinary placental infarction is difficult to determine. Here there is no retroplacental bleeding, although it is not uncommon to find in the same placenta both forms of infarct, that associated with retroplacental bleeding and that placed directly upon the decidua. Whether the ischaemia in the latter case is dependent upon a sudden and complete vascular constriction similar to that described in menstruation (Markee[31]) or upon thrombosis is unknown. It is true that thrombosis in the corresponding vessels is often present (Young[1]) but whether it is primary or secondary it is impossible to say.

The considerations set out above are in keeping with the view that the constitutional background to the abortion-toxaemia taint is hormonal. This constitutional implication is well expressed in those women in whom the reproductive history consists of an unbroken succession of abortions, premature births or stillbirths with toxaemia punctuating one or more of the vitiated pregnancies (recurrent pregnancy toxaemia, Young[3]). But there is not always such evidence of an intrinsic and continuing taint. For the recurrent phenomenon may first appear after there have been one or more normal pregnancies, while, in other cases, the toxaemic pregnancy may be the only morbid episode in a succession of healthy gestations (Case 10). These occasional toxaemic attacks are known to accompany such conditions as placenta praevia, where there are obvious factors making for massive placental degeneration, and twins and hydramnios where the same correlated factors of abortion and prematurity and toxaemia may also be local in origin. Finally, there is complete evidence in animals, and some evidence in man, that abortion may be caused by a deficiency of certain vitamins in the diet. Whether this connotes a direct and specific influence on the reproductive organs or an indirect influence through the endocrine glands is unknown.

Discussion—Essential Hypertension and Toxaemia

We have given some evidence in the preceding pages to indicate that a continuing toxaemia is associated with a continuing placental involvement. At the same time the argument has been based in the main on the clear correlation between massive placental involvement and severe toxaemia. In many patients with a continuing toxaemia of a mild degree there is no detectable placental disease. I have been unable to confirm the claims of some observers (e.g. Bartholomew and Colvin[4]), who state that placental pathology is always recognizable in such cases. Our attitude towards this question must be decided by the positive value we attach to the evidence available from the major phenomena. For it would seem to be clear that, in so far as the clinical manifestations on the minor scale are identical in quality (hypertension, oedema, albuminuria, headache, eye symptoms) with those exhibited by the graver and more fulminating forms, they must in many instances have a similar origin. There is thus implicit in our conception of the genesis of toxaemia the assumption that minor degrees of toxaemia may arise from placental changes which elude detection.

There is one clinical manifestation of toxaemia which demands special consideration in this connexion. Even major degrees of hypertension may be associated with an apparently healthy placenta. At the same time it is now recognized that in a majority of cases the hypertensive state found in pregnancy is to be identified with an intrinsic and essential hypertension which is carried into pregnancy or which first becomes manifest during pregnancy and that it is not evidence of a specific pregnancy toxaemia. The high incidence of persisting hypertension (50 per cent according to Corwin and Herrick[32]) found at the follow-up of toxaemic pregnancies is believed to be in the main of similar origin. There is no conclusive evidence that a specific toxaemia can produce a persisting hypertensive state. The careful observations of Reid and Teel[33, 34] and Chesley and his co-workers[35] indicate that women normal before a specific pregnancy toxaemia do not in subsequent life exhibit hypertension in a greater incidence than would be expected in women of the same age groups apart from pregnancy. Browne and Dodds[36] have come to a similar conclusion. At the same time there is evidence that hypertensive women are exposed to a greater risk of specific toxaemia than normal women. Browne and Dodds,[37] in a group of 234 women known to have hyper-

tension before the 20th week of their pregnancy, found 42 (17.9 per cent) to develop albuminuric toxaemia at a later stage of pregnancy.

The factors inherent in the hypertensive state which predispose to toxaemia remain to be determined. There is little reason to believe that the hypertension *per se* has a direct influence, still less for the extreme expression of this view that "eclampsia is a form of hypertensive encephalopathy that occurs in nephritis or other forms of toxaemia" (Fishberg[38]). (1) In the first place, the common type of pregnancy toxaemia, characterized by albuminuria and oedema occurring in the later months of pregnancy and of which eclampsia is the rare culmination, frequently does not exhibit any hypertension at any stage, or, alternatively, this may be only a late phenomenon. (2) All obstetricians of experience have records of eclampsia without hypertension. In the records of the Edinburgh Royal Maternity Hospital, out of 237 women with eclampsia who survived, there were 17 (7.1 per cent) whose blood-pressure did not rise above 120/80 and 48 (20 per cent) in whom the maximum was 140/90. (3) The haemorrhagic and necrotic lesion in the liver, which is characteristic of the fatal eclamptic case, is not found in hypertensive encephalopathy.

The production by Goldblatt[39] and others of a condition resembling essential hypertension by the partial occlusion of the renal artery in animals has prompted the suggestion that renal ischaemia may constitute an important element in the pathogenesis of pregnancy toxaemia, and that the necrotic lesions found in malignant hypertension and reproduced in the severe types of the experimental condition, may present some analogy to the necrotic lesions in eclampsia. Some investigators have claimed, by partial constriction of the renal artery or of the aorta above the origin of the renal arteries in pregnant animals, to have induced a condition resembling the toxaemia of pregnancy. The considerations set out in the preceding paragraph may, however, be urged against the essential relevance of these experimental claims. There is the further strong argument that pregnancy produces a fall in the experimental hypertension of dogs (Goldblatt, Kahn, and Hanzall[39]) and rats (Harrison, Grollman and Williams,[40] Page, Patton and Ogden,[41] and Wilson and Byrom[42]). Bearing on the same question are the observations of Kellar and Sutherland[43] that untoward effects do not follow the intravenous injection of renin into pregnant rabbits, and of Chesley *et al.*[44, 45] that in eclampsia and pre-eclampsia, unlike

essential hypertension, the renal blood-flow, as measured by the diodrast clearance, is characteristically normal.

Summary

1. Pregnancy toxaemia (pre-eclampsia and eclampsia) is preceded and determined by an abortion factor.

2. This operates by causing an interference with the maternal circulation in the placenta. Two alternative mechanisms can be recognized: (*a*) The stasis or complete arrest of the blood-flow is restricted to certain regions, resulting in a local area or local areas of placental degeneration. When, after complete arrest of the blood-flow, there is a sufficient interval of foetal survival with continuing circulation in the remaining placenta, the ischaemic area passes into the condition of infarction. (*b*) The vascular changes are widespread throughout the decidua (and sometimes also in the uterine musculature) and consist of dilatation and free blood extravasation, both of which may reach an extreme degree. The retro-placental bleeding is an extreme expression of this widespread vascular disturbance. In many instances (*a*) and (*b*) are found to have been in operation in the same placenta.

3. The toxaemia develops subsequent to the placental degeneration. It is related to the early stages of this process, and its severity is determined both by the extent of the placental involvement and by the interval during which the foetus survives *in utero* (and the circulation continues) between the onset and the maximal development of this involvement. Evidence has been given that at least half of the placenta may be thus compromised before foetal death occurs.

4. The relation of the toxaemia to the initial stages of the degenerative changes explains how after early foetal death or delivery the full extent of the placental involvement may not be visible to the naked eye or even to the microscope.

5. The above considerations explain the high incidence and the grave nature of the toxaemia found in concealed accidental haemorrhage, and, also, the apparent paradox that in many such cases there may not be the least evidence of toxaemia. The latter are explained by immediate massive involvement of the placenta resulting in immediate foetal death.

6. In concealed accidental haemorrhage (in which an extensive muscular lesion is also often present) an acute renal lesion with blood-stained urine, oliguria or suppression, and a rapidly

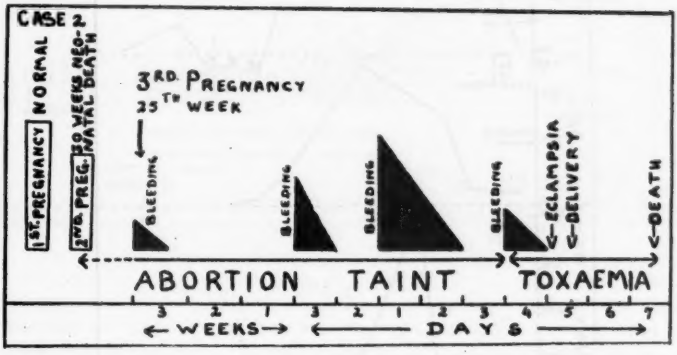

FIG. 1.

The abortion factor dates from 2nd pregnancy. It is manifest without toxaemia from the 25th week of 3rd pregnancy. It is *followed* by eclampsia at 28th week.

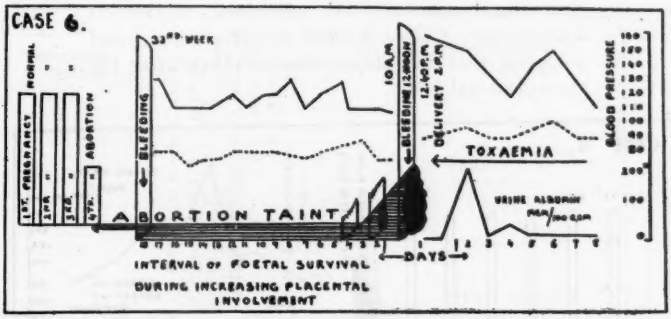

FIG. 2.

The abortion factor dates from 4th pregnancy and was evident without toxaemia at 32nd week of 5th pregnancy. The mild toxaemic manifestations at the 34th week clearly *follow* the minor placental episode which, the child being alive, is abruptly terminated by delivery.

J.Y.

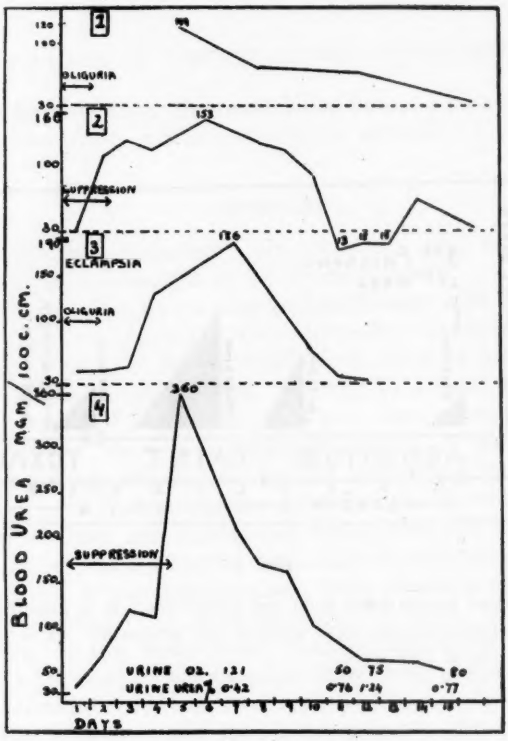

FIG. 3.

Acute renal deficiency in "concealed" accidental haemorrhage. Curves of blood urea levels in 2, 3 and 4 suggest that the phenomenon develops *after* the utero-placental lesion.

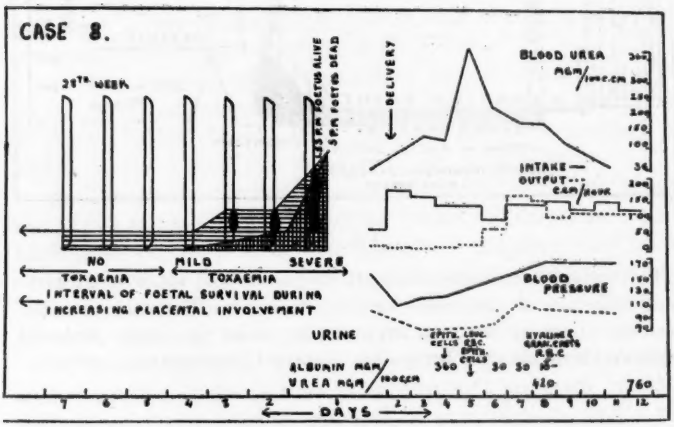

FIG. 4.

The placental degeneration antedates the toxaemia. The climax of the toxaemia follows the climax of the placental involvement; this was gradual and became massive before foetal death.

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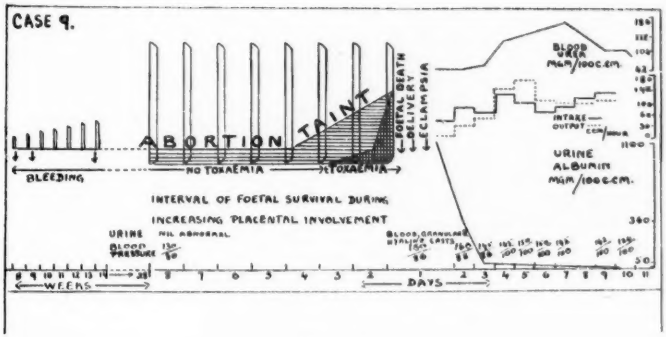

FIG. 5.

The abortion factor manifest at 8th, 9th and 14th weeks. The placental degeneration antedates the first evidence of toxaemia. The climax of the toxaemia follows the climax of the placental involvement; this was gradual and became massive before foetal death.

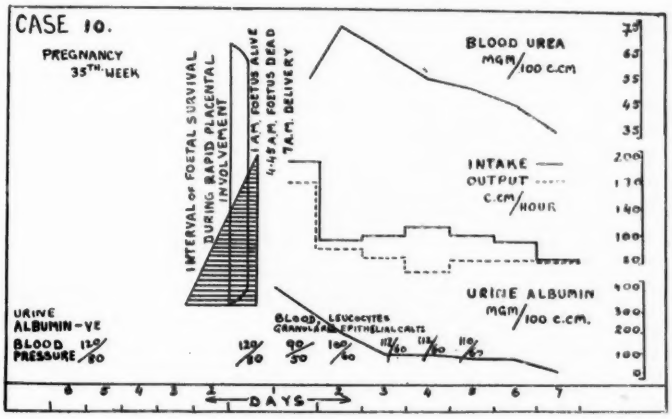

FIG. 6.

Five days before the patient was normal. The rapid placental involvement results in early foetal death. The toxaemic features are mild.

J.Y.

FIG. 7.

Habitual abortion. Decidua vera showing lacuna-like distension of vessels with free extravasation. 12 weeks. ×56

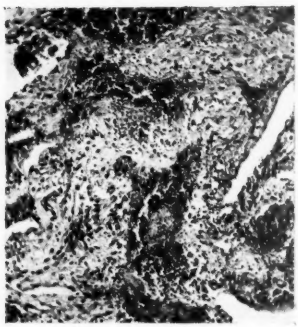

FIG. 8.

Concealed accidental haemorrhage. Decidua showing lacuna-like distension of vessels with free extravasation. 32 weeks. ×56

rising blood urea, may be superimposed on the typical pre-eclamptic or eclamptic phenomenon. The resemblance between this syndrome and the "crush syndrome" in regard to genesis, clinical features and morbid anatomy, has been analysed.

7. The correlation between the utero-placental lesion and toxaemia has in the main been recognized only in respect of the severe and major phenomena. A correlation has not been found between the placenta and the minor clinical manifestations of toxaemia and there is implicit in the argument the assumption that these may arise from a lesion which eludes our present methods of detection.

For the preparation of the diagrams I am indebted to my assistant, Dr. Meave Kenny, and of the microphotographs to Mr. C. V. Willmott of the Photographic Department of the British Postgraduate Medical School. This communication is published with the permission of the Medical Officer of Health, London County Council.

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Caesarean Section under Spinal Analgesia

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THE choice of an anaesthetic in patients requiring Caesarean section is a matter of paramount importance, and the primary consideration must be the degree of safety to mother and child accompanying its use. Of secondary, but nevertheless major, importance, is that which might be termed the operative comfort afforded to the surgeon. The ideal anaesthetic is one which satisfies all these three considerations.

In the course of the search for such an ideal, spinal analgesia has been given an extended trial, since it has certain definite advantages which may be summed up as follows:

For the Mother.

Marshall[1] quotes Rismondo as stating that spinal anaesthesia must be reckoned among the oxytocic drugs. Other references by Marshall are: "*On opère à blanc*" (Audébert); "The operation is rendered easy and elegant" (Brindeau).

"Diminished haemorrhage—this is the most outstanding feature of the operation when carried out under spinal anaesthesia. The uterine wound can be extended with safety and precision. Suturing is carried out while the organ is in a state of maximal retraction and the edges of the incision are quite anaemic. Increased solidarity of the union results, with all its advantages, immediate and remote. Manual removal of the placenta with its attendant dangers of increased loss of blood and infection is rarely called for. Atony does not arise, and delayed haemorrhage is an unusual complication." (Marshall.)

"The incidence of morbidity of genital origin was only half that of cases operated on under general anaesthesia." (Siegert.)

Marshall states that the effects on metabolism, liver and kidneys are negligible, and it may safely be used in patients in whom these organs are diseased, and in whom general anaesthesia might possibly prove fatal. He refers to the dynamic

effects of spinal anaesthesia on bowel peristalsis, and quotes Geller's belief "that a part of the lowered mortality in Caesarean section under spinal anaesthesia must be attributed to its action in this direction. Post-operative vomiting is rare, and intestinal atomy, meteorism, and ileus are all quite uncommon in the early puerperium."

Our own experience confirms all the above statements.

For the Infant.

The child is unaffected by the anaesthetic, and any marked degree of asphyxia is rare. Lobeline injected into the umbilical cord has been successful in the few cases met with in our series, no other treatment beyond the routine clearance of the air passages being required. We have not had any foetal deaths which could be attributed to the anaesthetic.

For the Surgeon.

Many of the above advantages make for operative comfort. In addition, the perfect relaxation of the abdominal muscles renders the approach to the lower uterine segment easy, and the placid abdomen greatly aids in the incision and suture of the opening into the uterus.

In spite of the undoubted advantages described above, it must be admitted that there has been considerable controversy regarding the safety of spinal analgesia. While some surgeons have expressed themselves as satisfied with it, others, after a longer or shorter trial, have condemned it, chiefly on account of the liability to sudden drop in blood-pressure, collapse, and death, which has occurred with startling rapidity, sometimes even before the operation has commenced, and that, too, in young woman whose health has been apparently perfect. Among other complications which have been cited are meningitis, paralysis, and severe headache.

We would here refer to a paper by Ashworth,[3] in which he gave as one of the indications for spinal anaesthesia, the operation of Caesarean section, and stated that "spinal anaesthesia produces excellent uterine contractions, thus diminishing haemorrhage, and also ensures that the infant, when born, is not anaesthetized."

Discussing the contra-indications, Ashworth said, "If the general condition of the patient cannot be improved by rest, warmth, intravenous saline injections, or ephedrine, until the

systolic blood-pressure has been raised to at least 90 mm. Hg, and any pre-existing dehydration remedied, then spinal anaesthesia should not be employed." The relevance of this warning to cases of antepartum haemorrhage from placenta praevia, for which condition Caesarean section is tending to become an increasingly frequent method of treatment, will at once be obvious. To the above restoratives should, therefore, be added the use of blood transfusion, which, now the blood-banks have been so widely established, should be as easy of application, in most cases, as any of the other measures, and is of far greater value than any for this particular condition.

Other contra-indications given by Ashworth were: "Certain forms of severe cardiovascular disease. (Types unstated.) Severe myocardial deficiency. Profound anaemia, and low blood-pressure." The most dramatic combined example of the last two is to be found in the severe loss associated with placenta praevia.

Ashworth also states that spinal anaesthesia should never be used unless the mental tranquillity of the patient is assured. Some interesting sidelights on this question will be mentioned later in connexion with Caesarean sections performed during air alarms.

Referring to premedication, Ashworth stresses the importance of ephedrine. "Forty-five minutes before operation, gr. $\frac{3}{4}$ of ephedrine should be given, except in cases of hyperpiesis, in order to combat the fall in blood-pressure which often accompanies spinal anaesthesia. Ephedrine is a slow-acting drug, and the vasoconstrictors are paralysed long before the ephedrine is absorbed from the subcutaneous tissues."

Ashworth's paper was followed by a spirited correspondence, in which several surgeons and anaesthetists took part, and the divergence of opinion as to the safety of spinal anaesthesia is so plainly revealed that an apology is not made for quoting freely from these letters.

Spencer[3] wrote, "In my book on 'Caesarean Section' (1927), I stated that I had never employed spinal anaesthesia in cases of Caesarean section, on account of the increased risk to the mother which it entails. During the last 10 years many cases have been published in which death or severe disabilities such as meningitis, paralysis, severe headache, were due to this method of treatment." He quoted 2 cases described in *Bull. de la Société d'Obstétrique et de la Gynécologie de Paris* (July, 1937) of low Caesarean section in young healthy women in which fatal syncope occurred within 1 to 3 minutes of the

spinal injection. During the subsequent discussion, Professor Brindeau and Professor Brouha stated that they had had several fatalities, and the latter had in consequence abandoned spinal anaesthesia in cases of Caesarean section. Professor Voron alluded to the special bulbar sensitivity of women in labour to the action of cocaine compounds, and added "undoubtedly we ought to give up the employment of a mode of anaesthesia which otherwise possesses such incontestable advantages."

Spencer then quotes DeLee thus: "Kronig said spinal anaesthesia is dangerous in pregnancy and labour, and present experience with all the drugs sadly confirms this." The drugs specifically named by DeLee[4] are stovaine, spinocaine, tutocaine and procaine. Spencer concludes "for the foregoing reasons I was sorry to find, in Dr. H. K. Ashworth's important article on spinal anaesthesia, Caesarean section given as an indication for that method of anaesthesia."

Luker[5] said, "I have used spinal anaesthesia for Caesarean section for many years and am satisfied with its advantages, not only when ordinary obstetric indications are present, but especially when heart disease or lung disease is present. My anaesthetist, Dr. J. C. A. Norman, and I have found it free from danger under the technique we have evolved—(1) premedication, (2) spinocaine, which is given with the most rigid antiseptic precautions, and with meticulous attention to many details. We are convinced of the safety and advantages of this method."

Lloyd-Williams[6] stated: "Of 120 Caesarean sections performed during the years 1935 to 1937, 44 were done under spinal anaesthesia with no maternal deaths. There were no cases of paralysis or meningitis, and the incidence of any degree of headache was not marked. The anaesthetic used does not belong to the cocaine group. A 1 in 2000 solution of light percaine was used, with a preliminary injection of ephedrine to combat the fall of blood-pressure. The excellent contractions of the uterus seen under spinal anaesthesia lead to a greatly diminished loss of blood, and the baby is entirely unaffected by the anaesthetic."

Coleman[7] "used regularly to perform many Caesarean sections under stovaine spinal anaesthesia, and never saw any ill-effects in either mother or child."

Kidd[8] relates the following alarming experience: "While I have done several hundred general surgical operations under spinal anaesthesia without an anaesthetic death, I had, using the same technique, two deaths in a series of 18 Caesarean sec-

tions. Both patients were in good condition before the anaesthesia, and both collapsed and died a few minutes after its introduction, and before the operation was begun. In one case spinocaine was used, and in the other percaine. I have now abandoned the use of spinal anaesthesia for this operation."

Referring to Luker's letter, Kidd says, "Dr. Gordon Luker does not state how many cases he has done, but if his statement that he has never yet found a fall in blood-pressure is literally correct, then either he has not taken the pressure during the operation, or he has a truly remarkable and unique technique of which it would be interesting to have further details. While experienced obstetricians may have evolved a special technique, I think that surgeons who only perform this operation occasionally should bear in mind the fact that there is an increased risk in the use of spinal anaesthesia in advanced pregnancy." It will be noted that although Kidd cavils at Luker for not stating the number of his cases, he himself, though saying he used the same technique for his obstetrical and general surgical cases, does not state what that technique was, or whether ephedrine or other drug was used to counteract the fall in blood-pressure, or even, in the case of the second death, whether the percaine was of the light or heavy variety.

Marshall, in his book on "Lower Segment Caesarean Section," records that out of 246 sections, 112 were performed under spinal anaesthesia, the drug used being chiefly stovaine, in a dosage of about 0.8 c.c. He says, "My own experience leaves me in no doubt that spinal anaesthesia is particularly dangerous in Caesarean section. On 3 occasions I have encountered severe degrees of collapse; in another patient breathing ceased, the pulse was imperceptible, and for some moments I acted on the presumption that she was dead. On several other occasions the condition of the patient caused me considerable anxiety, and brought the operation to a temporary standstill." Marshall came to the conclusion that "any obstetrician who sets out to perform a large series of Caesarean sections under spinal anaesthesia must be prepared to face a possible maternal mortality of not less than one per cent due to this cause alone." Marshall's experience is completely opposed to our own, as will be seen from our case reports.

In a review of current literature (*Journ. of Obstet. and Gynaecol. of the Brit. Emp.*, Oct. 1940) Professor Sebrechts[9] is quoted as having recorded 115 cases of Caesarean section under spinal anaesthesia without a fatality, the anaesthetic being percaine,

1 in 1500. "For Caesarean section 10 c.c. are enough, although 20 c.c. is the average dose for non-pregnant women." He mentions "the special susceptibility of parturient women."

Van der Post[10] describes 3 cases in which light percaine given by the Etherington-Wilson technique had been used in pregnancy, 2 being for Caesarean section, and one for ruptured ectopic gestation. One case of Caesarean section and the ruptured ectopic died, and the other Caesarean section nearly died. In our view the information given by Van der Post is insufficient to justify the responsibility for death in 2 cases and a fright in the third (Etherington-Wilson's own phrase, and very apt!) being placed upon either the technique or the spinal anaesthesia itself. In none of the case-reports is any indication given of the amount of blood lost at operation. In the first case, the indication for Caesarean section is not given, though the patient was stated to be "thin, and very sallow in complexion, and looked rather ill." As the abdomen was being closed, signs of air hunger and an almost imperceptible pulse developed. These signs would fit a case of haemorrhage, but there is no mention of any such loss, either antepartum, or during operation, nor is there a record of the haemoglobin percentage before section. It must be noted that the patient had passed through the most important stages of the section before these signs developed.

Van der Post's second case is remarkable in that the patient actually passed successfully through the operation, the anaesthetist had left before the completion of the section, having first assured himself that the patient's condition was satisfactory, and the surgeon had been seen off the premises by the house-surgeon, who also had satisfied himself as to the patient's condition before leaving her. He was recalled to the theatre, where he found her dead on the Trendelenburg trolley.

In the case of the ruptured ectopic gestation, information is not given as to the amount, if any, of intraperitoneal bleeding which occurred, either before or during operation, nor of the haemoglobin percentage before laparotomy.

At the end of his paper, Van der Post makes the following statement, which I must confess puzzled me. "At the time the above spinal injections were administered, it did not occur to me to ask the patient whether she was menstruating, or whether she had just passed through her menses." Cases 1 and 2 were presumably at or near term. Why, therefore, should this question of menstruation be raised at all? Van der Post goes on to say, "it would be interesting to hear from one of your readers

whether the menstrual flow, or any haemorrhage for that matter, affects the specific gravity of the cerebro-spinal fluid." One of the contra-indications to spinal anaesthesia is profound anaemia, another is low blood-pressure, and both may be present in the same case as a result of haemorrhage. The importance of blood transfusion in such cases is evident.

Mallison[11] also describes the case of a patient with ruptured ectopic gestation who died under spinal anaesthesia, which was decided upon because "absolute relaxation was desired owing to the very fat belly." The history of this case includes continuous slight bleeding for 10 days, and a heavy loss the day before operation. Mention is not made of the amount, if any, of intraperitoneal bleeding, but among the measures adopted when the patient's condition became serious was—"Patient de-Trendelenburged. This was done apparently because it was considered that blood pressing on the diaphragm was helping to embarrass respiration." Presumably this blood was intraperitoneal, and the question arises whether the patient died of haemorrhage or spinal anaesthesia.

Mallison, discussing the results on the intra-abdominal pressure of the sudden release of a large abdominal tumour (i.e., the emptying of a gravid uterus at term) says "no mention seems to have been made of there being any danger to be apprehended from using a spinal method for ovarian cystectomy or the removal of large fibroid uteri." We shall describe later a case of 30 weeks' pregnancy complicated by an ovarian cyst containing 22 pints of fluid which was successfully dealt with under spinal anaesthesia without disturbing the pregnancy, which went on to term and spontaneous delivery.

Murad and Parhad[13] stated that the last 50 cases requiring Caesarean section in the Royal Hospital, Bagdad, had been given spinal anaesthesia as a routine, with no deaths referable to the anaesthetic (tutocaine dissolved in the patient's cerebro-spinal fluid).

The above references, while showing the difference of opinion as to the merits of spinal anaesthesia in pregnancy, are sufficient to justify certain conclusions.

1. The use of spinal anaesthesia confers certain definite advantages on the mother, child and operator.

2. There are definite contra-indications to its use, some of which, e.g. anaemia and low blood-pressure, are capable of being surmounted by appropriate measures.

3. It is associated with a drop in blood-pressure, which, if

not anticipated, may lead to alarming and sometimes fatal results. The distribution of the blood supply peculiar to the pregnant state, its disturbance consequent upon the emptying and subsequent retraction of the uterus, and the alteration of the intra-abdominal pressure following the delivery of the child, must be remembered when considering the question of circulatory changes.

4. Some authorities (Voron) think women in labour have a special bulbar sensitivity to cocaine compounds, while others (Kronig, DeLee, Marshall) think spinal anaesthesia is dangerous in both pregnancy and labour. A number of fatalities have been reported, also a number of alarming experiences.

5. A variety of drugs has been used, some related to cocaine (stovaine, spinocaine, tutocaine), others not so related (light percaine). We have not seen any reference to the use of heavy percaine for Caesarean section.

A Review of 121 Cases of Caesarean Section Performed Under Spinal Anaesthesia

We have used spinal anaesthesia as the anaesthetic of choice for Caesarean section since April, 1938. We would state here that we consider a spinal anaesthesia to be successful only if it has not to be supplemented by some other form of anaesthesia, such as gas and oxygen, with or without ether. Taking this as the criterion, we have, up to date, performed 121 Caesarean sections under successful spinal anaesthesia without a death referable to the anaesthetic. The only death in the series occurred on the 9th day after the operation, from pulmonary embolism. (Table 2, case 16.) Eight other patients were given spinal anaesthetics, but as in 6 of them the anaesthesia did not rise to the umbilical level, and in 2, failed more or less completely, these patients were given gas, oxygen and ether through Boyle's apparatus. As their cases do not conform to the standard described above, they are not included in the series.

Drugs Used, and Technique of Administration

Among our earliest cases, 2 of the patients were given light percaine (Table 1, cases 2 and 6) and one stovaine (Table 3, case 17). The remainder, 118 in all, were given heavy percaine.

Percaine is described by the makers, Ciba, Limited,[12] as a complex amine derivative of quinoline, the full nomenclature

being "the hydrochloride of abutyloxycinchoninic acid diethylethelene diamide." It is unrelated to the cocaine compounds. Heavy percaine (Ciba) is a hyperbaric solution, 1 : 200, with 6 per cent glucose, and is put up in sterile ampoules of 3 c.c. A considerable amount of information as to the properties of percaine will be found in the Ciba Handbook, No. 2.

Simplicity of technique must be an advantage for any form of spinal anaesthetic, for any type of operation, and for any class of patient. It is particularly desirable in pregnant women, and especially so in cases of placenta praevia, in which undue movement of the patient may precipitate a loss at a very awkward moment. The technique of administration of heavy percaine could hardly be simpler.

Premedication. Marshall states, "Morphine, hyoscine, and all respiratory depressants are dangerous, and should be omitted. (Preissecker, Mayer, Thiessen.) The 2 patients in whom the most alarming degrees of collapse occurred were among the very few whom I had prepared with these drugs." Among our patients, many of the "trial labours" had been given omnopon gr. 1/3, with scopolamine gr. 1/150, and the latter sometimes repeated, as part of our support to the patient during the course of the trial. This, however, is not the same as the administration of sedatives as adjuncts to the anaesthetic itself, and Caesarean section has not been carried out within 2 hours of such drugs having been given. The possible effect of the drugs in producing apnoea in the infants, the most important contraindication, would, therefore, be negligible. Apart from the above, we have given 2 drugs only, as premedication. Atropine gr. 1/100, was given as a routine in every case, not as an adjunct to the spinal, but in the event of the spinal failing to produce the required height of anaesthesia, and a general anaesthetic becoming necessary. Ephedrine gr. 3/4 was given to all patients, to combat the drop in blood-pressure. For some time this was given as soon as the spinal anaesthetic had been injected. Latterly, however, it has been administered with the atropine 45 minutes before the operation, as recommended by Ashworth. Apropos of the need for sedatives, Ashworth has stated that "spinal anaesthesia should never be used unless the mental tranquillity of the patient is assured." It may be that in patients about to undergo Caesarean section, the knowledge that they are to be quickly, safely, and painlessly delivered suffices to assure such mental tranquillity, especially when section puts an end to what might have been a tedious trial labour.

But among our patients, 55 were not in labour when the operation was performed, and in these there was no such influence. None of these women received any premedication other than atropine and ephedrine. In this connexion, our experience of performing Caesarean sections during air raid alarms and actual raids is both interesting and instructive.

Five sections were carried out under the above conditions. The period in question covered the months of August, September and October, 1940, when day-time alarms and air battles were frequent, and night raids occurred with almost monotonous regularity. Surely no greater mental strain could be imposed on a patient than to be prepared for and undergo the operation of Caesarean section to the accompaniment of the wailing of sirens, the droning of planes overhead, or the reverberating crashes of an intense barrage. That spinal anaesthesia does not produce unconsciousness might well be thought disadvantageous in such circumstances. None of these patients asked "to be

Table Case No.	Conditions	Labour	Time of section	Baby
1 53	Air raid warning during preparation and section. Barrage during previous nights.	Trial 144 hours	12 noon	Living, general condition good
1 54	Air raid warning during section. Heavy barrage.	Trial 37 hours	7.50 pm.	Living, general condition good
1 55	Air raid warnings during preparation and section. Barrage during section.	Trial 17 hours	5.30 p.m.	Living, apnoea and distress
1 56	Admitted, prepared, and operated on during heavy barrage. Foetal distress from prolapsed umbilical cord.	4 hours	4.0 a.m.	Living, apnoea and distress
1 57	Air raid warning as section began. Planes overhead. Continuous cheery conversation between patient and operator all through the operation. A remarkably brave patient.	Trial 35 hours	12 noon	Living, general condition good

put to sleep," nor to be given a sedative. Their courage and calm confidence were beyond praise, and I believe they were concerned only with the welfare of their babies, and had no thought for themselves.

The preceding table gives some idea of what these mothers went through. It will be seen that there were 4 trial labours, of 144, 37, 17, and 35 hours respectively, during which the patients were supported by omnopon and scopolamine. All these had already gone through one or more nights disturbed by anti-aircraft barrages, in addition to having their sections performed under the same conditions. The fifth had already had one Caesarean for contracted pelvis, and was admitted on the present occasion at midnight, during a barrage, in the early stages of labour. The umbilical cord prolapsed about 3 a.m. and the barrage was still on when the operation was done. All these patients had live babies.

The above is a remarkable record of what can only be termed superhuman courage and endurance, and it was very gratifying that all 5 of the mothers were rewarded by live babies.

Technique of the Administration of Heavy Percaine. The patient is placed on the operating table in the left lateral position, her head and knees being approximated as closely as possible, the ward sister helping her to maintain this position. Two syringes are loaded, one with novocaine, 2 per cent, the other with heavy percaine. The area is prepared with spirit, and the space between 3rd and 4th lumbar vertebrae is defined. An intradermal weal is raised with novocaine, and the needle then pushed in, at the same time novocaine is injected into the track. The spinal needle is then passed into the theca, and the required quantity of heavy percaine injected without aspirating cerebro-spinal fluid. The site is sealed with an elastoplast dressing, and the patient turned on her back. The head and shoulders are raised, and the table tilted into a slight Trendelenburg position, sufficient to bring the 7th dorsal vertebra, the most dependent part. A tilt of about 7° is usually required. This position is maintained for 5 minutes, after which the table is returned to the horizontal. The patient's head, however, is kept raised throughout the operation. Anaesthesia almost up to the ensiform is obtained.

The needles we use for intraspinal injection are Allen and Hanbury's spinal needles, No. 16 or 17, with trocar and short bevel.

The time of commencement of the section is usually about

15 minutes after the injection of the spinal anaesthesia, the interval being taken up by 5 minutes in the Trendelenburg position, the fixing of the anaesthetic screen, iodizing the operation area, and draping the patient. A number of the cases of placenta praevia were examined under the spinal anaesthesia to confirm the diagnosis, the patient being placed in the lithotomy position for this purpose. The length of anaesthesia obtained is amply sufficient for this and for a lower segment section and sterilization by excision of both Fallopian tubes, without the need for the slightest hurry.

It will be seen that the amount of movement to which the patient is subjected in the above technique is small, and the assistance of nurses accustomed to the technique can reduce it to an almost negligible minimum. A word of warning in regard to cases of placenta praevia is necessary. We do not allow these patients to make any effort to assume the lateral position prior to, or to resume the supine position subsequent to, the injection of the spinal anaesthetic. They are placed in the required attitudes by the nursing staff, of whom 3 are necessary, one taking the legs, one the hips, and one the head and shoulders. This precaution is taken to obviate the possibility of a sudden rise in intra-abdominal pressure from muscular exertion, which may result in separation of the placenta, with bleeding at an embarrassing moment. Similarly the approximation of the patient's head and knees should not be too vigorous. We have had one such incident, in which a patient with a central placenta praevia suddenly began to bleed profusely at the moment when the spinal needle had been introduced. (Table 2, case 2.) Fortunately, her condition was very good, 2 blood donors and plenty of assistance were at hand, and all preparations for blood transfusion had already been made. The injection was completed. Section and transfusion were commenced simultaneously, the first 20 ounces of blood being run in as rapidly as was compatible with safety. A further 30 ounces were given, making 50 ounces in all. So far as could be estimated, the patient had lost about 40 ounces. Her haemoglobin the week following section was 78 per cent, and she was discharged well on the 21st day, breast-feeding her baby. It was a very anxious moment, particularly as this was her 6th pregnancy, and she had had no previous live child. It is interesting to note that in spite of such a loss, and the administration of a spinal anaesthetic, she did not show the slightest sign of collapse, but maintained a good colour and steady pulse throughout the section. The prompt

blood replacement was undoubtedly responsible for this, which shows the value of being prepared for such an emergency. We never operate on a case of placenta praevia without having a supply of blood available in the theatre.

Observations Made During Caesarean Section Under Spinal Anaesthesia.

The induction of spinal anaesthesia is not unpleasant. Little is felt other than the first prick of the needle when raising the intradermal weal. The coughing, straining, and feeling of suffocation so often associated with a general anaesthetic are eliminated. The excursions of the abdomen due to respiratory stertor under general anaesthesia are absent under a spinal anaesthesia, the abdomen being placid.

Complete relaxation of the abdominal musculature is obtained. This permits the abdominal walls to be lifted off the uterus when packing off the peritoneal cavity, the packs being placed in position, not pushed. Exposure of the lower segment is easily obtained by means of a Doyen's retractor, and the peritoneal and uterine incisions can be made with ease and under observation, and the subsequent closure is similarly facilitated.

We can confirm the observations of other writers (Marshall, Audébert, Rismondo *et al.*) as to the effects on the uterus and bowel. Haemorrhage is very unusual except from the placental site when situated in the lower uterine segment, and that not often. Two patients (Table 1, cases 42 and 49) had a free loss from a placental site in the normal situation, and 3 patients had to be packed to control haemorrhage from placental sites in the lower segment. (Table 2, cases 2 and 18, and Table 3, case 8.) We nearly always give a routine injection of pitocin 1 c.c. into the uterine muscle after extraction of the child. Some patients have experienced nausea, usually about 25 minutes after injection of the spinal, which is about the time of extraction of the child. This has passed off on the administration of oxygen and carbon dioxide from the Boyle's apparatus, which is always ready at the head of the table. It is, no doubt, brought about by a slight fall in blood-pressure.

Variation in Blood-Pressure. Most of the deaths under spinal anaesthesia have been attributed to collapse following a sudden marked drop in blood-pressure. That there may be such a fall must be admitted. It is stated to be greater with some drugs than others, and Messrs. Ciba, Ltd. quote Howard Jones as stating that the fall of blood-pressure following the injection of percaine was not so

great as that seen with procaine and stovaine. They also quote the observations of Keyes and McLellan, who found in 43 cases in which procaine was injected an average maximal fall of 31 mm. Hg, while in 41 percaine cases the average maximal fall was only 18 mm. Hg. If the fall in blood-pressure is to be explained by the paralysis of the vasoconstrictors, it follows that great care is necessary to guard against too steep a Trendelenburg tilt, with a consequent too high anaesthesia and wider range of vasoconstrictor paralysis, and that ephedrine, in order to combat this fall, should be given before, not with or after, the spinal. The influence of haemorrhage during section as an additional cause of a fall in pressure will be readily appreciated, the type of case in which it is most likely to occur being that of placenta praevia. In performing the lower segment operation in such cases, the placenta, if situated anteriorly, has sometimes to be cut through, and an appreciable loss of blood may occur before the child is delivered. Further, after the placenta has been delivered, there may be a continuous oozing from the placental site, very deceptive in its amount, which the relatively inefficient retractile power of the lower segment fails to control. DeLee, in speaking of such cases, recommends the alternatives of suturing the bleeding sinuses, or tamponade. Unless, however, the bleeding area is small, and can be brought easily into view, much valuable time and blood may be lost before the oozing can be controlled by suture, and we believe that prompt and

TABLE I. CASE NO. 73.

Time	Blood-pressure		Remarks
9.0 p.m.	128/76		Trial labour, 18½ hours
9.30 ,,		Ephedrine	
10.15 ,,	120/88	Spinal given	
10.20 ,,	110/85		
10.25 ,,	110/75		
10.30 ,,	110/80	Incision	
10.35 ,,	105/75		
10.40 ,,	100/85	Delivered	
10.45 ,,	115/85		
10.50 ,,	110/78		
10.55 ,,	98/80	Coramine, 1.7 c.c.	
11.0 ,,	112/78		
11.10 ,,	110/75		
11.15 ,,	108/78		
11.20 ,,	105/75		

efficient packing of the lower segment is the best method to adopt. The decision to pack must be made before the loss has assumed dangerous proportions.

We give below the serial blood-pressure of some of our most recent cases. Particulars of the sections will be found in the corresponding tables.

TABLE I. CASE NO. 74.

This patient was of very asthenic type, and had been in hospital for several weeks during this pregnancy with bronchitis. Her blood-pressure was low when first seen at the clinic, and she was put on iron and vitamins. She was admitted for rest and further treatment a week before term. She had had two previous Caesarean sections for contracted pelvis, the second having been done under spinal anaesthesia. Her blood-pressure 2 days before the third section was 98/58. Coramine 12 m. was given three times a day before section, and 1.7 c.c. the morning of the section. The blood-pressure rose to 108/58. Ephedrine was given as usual 45 minutes before the spinal anaesthetic.

Time	Blood-pressure		Remarks
12.10 p.m.		Spinal	
12.20 ,,	115/80		Lower segment Caesarean section and sterilization by the excision of the Fallopian tubes. No headache. Slight abdominal distension, relieved by eserine and enema.
12.30 ,,	103/75	Incision	
12.40 ,,	100/75	Delivered	
		Coramine 1.7 c.c.	
12.50 ,,	140/85		
1.0 ,,	120/80		
1.10 ,,	120/80		
1.20 ,,	115/75		
1.30 ,,	110/65		
1.40 ,,	110/65		

TABLE I. CASE NO. 75. *See special description of this case,* p. 272.

Time	Blood-pressure		Remarks
8.45 a.m.		Ephedrine	
9.45 ,,	135/80	Spinal	
9.55 ,,	100/58	Vomited. O_2 and CO_2	
10.5 ,,	90/58	Incision. Coramine	
10.15 ,,	70/50	Coramine. Ephedrine	Hysterical weeping.
		Operation stopped	
10.25 ,,	130/75	Delivered	Further weeping.
10.35 ,,	130/75		
10.45 ,,	120/70	Abdomen closed	
12.15 p.m.	110/70	Condition good	Still lachrymose.

TABLE 2. CASE NO. 20.

Time	Blood-pressure		Remarks
4.0 p.m.	112/80	Ephedrine	Operation and convalescence uneventful.
4.30 ,,	128/84		
5.0 ,,	140/98	Spinal	
5.5 ,,	140/98		
5.10 ,,	138/98	Incision	
5.15 ,,	138/92	Delivered	
5.20 ,,	110/80		
5.25 ,,	142/98		
5.30 ,,	150/100		

TABLE 3. CASE NO. 19.

Time	Blood-pressure		Remarks
10.0 a.m.	124/74	Ephedrine	Operation and convalescence uneventful.
10.45 ,,		Spinal	
10.50 ,,	90/70	Ephedrine	
10.55 ,,	74/64		
11.0 ,,	110/80	Incision	
11.5 ,,	110/84	Delivered	
11.10 ,,	110/80		
11.15 ,,	94/74		
11.20 ,,	116/80		
11.25 ,,	120/78		
11.30 ,,	120/78		
11.35 ,,	120/84		

TABLE 2. CASE NO. 19.

Time	Blood-pressure		Remarks
10.5 a.m.		Ephedrine	Lower segment Caesarean section for marginal placenta praevia. Severe loss at 28th week. Blood transfusion of 90 ounces including 36 ounces concentrated cells during subsequent 6 weeks, before section.
10.10 ,,	124/80		
10.50 ,,	110/80	Spinal	
11.15 ,,	100/70	Incision	
11.20 ,,	108/74	Delivered	
11.35 ,,	138/88		
11.40 ,,	120/86		
11.45 ,,	136/80		
11.50 ,,	136/86		
11.55 ,,	108/78		

TABLE 3. CASE NO. 20.

Time	Blood-pressure		Remarks
9.30 p.m.	110/80		Lower segment Caesarean section
9.45 ,,		Ephedrine	for obstructed labour due to
10.23 ,,		Spinal. Ephedrine	dermoid ovarian cyst. Ovario-
10.30 ,,	130/96		tomy performed after comple-
10.35 ,,	130/80	Incision	tion of section. Pituitrin in-
10.40 ,,	136/90		jected into the uterus after
10.45 ,,	134/92		delivery.
10.50 ,,	110/80	Delivered	Note sustained rise in blood-
10.55 ,,	136/90		pressure after this.
11.0 ,,	136/94		
11.5 ,,	130/90		
11.25 ,,	140/90		

TABLE 3. CASE NO. 21.

Time	Blood-pressure		Remarks
2.0 p.m.	140/90	Ephedrine	Note heavy drop in systolic
2.5 ,,	138/90		pressure after spinal anaesthetic
2.40 ,,	150/110	Spinal	with moderate rise after second
2.45 ,,	145/90		dose of ephedrine, and the
2.50 ,,	70/50	Ephedrine	marked and sustained rise after
3.0 ,,	70/50	Incision	delivery, which we attribute to
3.5 ,,	78/50		the use of 1 c.c. pituitrin into
3.7 ,,	116/86	Delivered	the uterine muscle; this was given
		Pituitrin into uterus	to obtain the combined pressor and utero-dynamic effect.
3.13 ,,	148/96		In spite of the heavy drop in
3.18 ,,	136/70		blood-pressure, the patient did
3.23 ,,	136/76		not show any sign of it.
3.28 ,,	146/90		
3.33 ,,	148/88		
3.38 ,,	156/98		

TABLE 2. CASE NO. 17.

Time	Blood-pressure		Remarks
1.30 p.m.		Ephedrine	Lower segment Caesarean section for central placenta praevia. Haemoglobin after section 61 per cent. Blood transfusion 40 ounces.
2.25 ,,	130/85	Spinal	
2.35 ,,	145/80		
2.40 ,,		Incision	
2.45 ,,	130/85		
2.50 ,,		Delivered	
2.55 ,,	135/85		
3.10 ,,	120/75		
3.20 ,,	125/80		

TABLE 2. CASE NO. 18.

Time	Blood-pressure		Remarks
11.15 a.m.	130/80	Ephedrine	Lower segment Caesarean section for central placenta praevia. Note heavy drop in blood-pressure after spinal anaesthetic, rise after second dose of ephedrine, followed by second drop with loss of 20 ounces, and final rise after blood transfusion. Uterus was packed to control loss. The only clinical sign of the drop in pressure was slight pallor. There were no signs of collapse. Condition next day excellent.
12.0 md.		Spinal	
12.10 p.m.	78/50	Ephedrine	
12.20 ,,	75/55	Incision	
12.30 ,,	98/60	Delivered	
12.45 ,,	68/45	20 ounces loss	
1.0 ,,	85/65	Abdomen closed	
1.10 ,,	90/70	Blood transfusion	
1.45 ,,	102/78		
7.0 ,,	130/80		

TABLE 3. CASE NO. 18.

Time	Blood-pressure		Remarks
2.0 p.m.	128/78	Ephedrine	Age 44 years. Fibroid uterus. First child stillborn. Very apprehensive about this baby. In hospital 12 weeks with pain in fibroids (red degeneration). Very mild post-operative headache.
2.30 ,,	118/78		
2.35 ,,		Spinal	
2.40 ,,	100/50		
2.50 ,,	110/68	Incision	
2.55 ,,		Delivered	
3.0 ,,	135/68		
3.10 ,,	120/78		
3.20 ,,	124/78		
3.30 ,,	115/82	Abdomen closed	
3.40 ,,	120/80		

We used not to register the blood-pressure as a routine during section, but relied on colour and pulse-rate, which the ward sister watched. Pressure readings have now been made part of the routine, with the obvious advantage, as seen in some of the above tables, that further steps to combat a fall can be taken at an early stage.

This drop in blood-pressure, which appears to vary greatly in different women, is undoubtedly the most important single factor to be considered when using spinal anaesthesia, and we would again refer to Ashworth's dictum that "until the systolic blood-pressure has been raised to at least 90 mm. Hg, then spinal anaesthesia should not be employed." We think the figure of 90 mm. Hg is too low, and suggest that 105 mm. Hg should be the minimum, and would prefer to employ such an anaesthetic as gas, oxygen, and ether if this figure could not be attained, especially in cases of placenta praevia associated with a recent heavy loss. To use spinal anaesthesia in patients who are "bad risks" is not only adding a further risk, but brings unjust discredit on the spinal anaesthetic. Fatalities in such circumstances should be attributed to unwise choice of anaesthetic rather than to the anaesthetic itself. Ashworth stated that "spinal anaesthesia is almost always the sure means of killing the moribund."

Mallison, after discussing the diminished CO_2 combining power and increased CO_2 content of the blood in pregnancy, said, "one would expect a greater fall of blood-pressure to take place as the result of the administration of spinal analgesia in the pregnant than in the non-pregnant patient. These considerations are certainly suggestive of the likelihood of trouble arising from the combination of pregnancy and spinal analgesia." Earlier in the same paper he says, "The question is not merely one of an increased splanchnic vascular bed and its dilation under the influence of spinal nerve paralysis, nor yet one of the presence of a large abdominal tumour and the results on the intra-abdominal pressure of its sudden release. Mention does not seem to have been made of there being any danger to be apprehended from using a spinal method for ovarian cystectomy or the removal of large fibroid uteri." We are able to record a case in which a large ovarian cyst complicating a pregnancy of 30 weeks was successfully operated upon under heavy percaine.

Mrs. W. J., primipara, aged 30, was seen at our antenatal clinic for the first time when 30 weeks pregnant. She had that

week come by air from the Isle of Man. Her history was of 30 weeks' amenorrhoea, that she had felt foetal movements, that her body had been getting thin, her legs were swollen, and her abdomen was very large. On examination, foetal parts could easily be felt of a size corresponding to the period of amenorrhoea. The abdomen, however, was enormous, and there was a marked fluid thrill everywhere above the umbilicus, obviously outside the uterus. She was in great discomfort, but heart and lungs, blood-pressure and urine were all normal. She was admitted to hospital, where a radiograph confirmed the size of the foetus. Heavy percaine was administered by the usual technique, and a right ovarian cyst was found lying above and behind the uterus. The cyst was first reduced in size, 12 pints of fluid being removed by trocar, and was then removed, being found to contain a further 10 pints, making 22 pints in all. She gave no cause for anxiety during the operation, her convalescence was quite uneventful, and she went to term, being delivered spontaneously 9½ weeks later of a living child weighing 6 pounds.

In this case, a very large abdominal tumour was removed, with a corresponding influence on the intra-abdominal pressure, in the presence of a fairly advanced pregnancy, which Mallison accounts a contra-indication of spinal analgesia, without the slightest sign of any untoward happening, under heavy percaine.

The Condition of the Infants.

The number of infants delivered was 123, of whom 5 were lost (stillborn, 1, died, 4), giving an uncorrected overall infant mortality of 4.06 per cent.

The infant mortality assessed according to the indication for section is as follows:

Indication	Cases	Infant losses	Mortality
Trial labour and disproportion ...	75	1	1.33 per cent
Placenta praevia	20	2	10.0 ,,
Miscellaneous	21	2	9.52 ,,
Cardiac disease	2	nil	nil
Toxaemia	3	nil	nil

In assessing the infant mortality in toxaemic cases, however, reference to the tables will show that 8 other mothers in addition to the above had toxaemia complicating the condition for which

section was performed, namely, Table 1, cases 33, 34, 52, 58, 70, and Table 3, cases 12, 14, 16 (including one set of twins). Of these 9 babies, 2 were lost, but it is not possible to assess the influence of the toxaemia on these deaths. Uncorrected infant mortality in 11 toxaemias (12 babies) is 16.6 per cent.

Apart from those lost, 4 babies who survived gave cause for anxiety at birth (Table 1, cases 56, 63, 55, 23). Two were due to malposition of the umbilical cord, the 3rd to foetal distress after a trial labour of 17 hours, and the 4th to a peculiar epileptiform attack which the mother had just before the child was delivered. All recovered after injection of lobeline 1 c.c. into the cord, and intra-nasal oxygen and carbon dioxide. None of the other infants gave us the slightest anxiety, and it is safe to say that heavy percaine does not appear to have any deleterious effect on the infants.

Post-operative Complications.

Headache. Two patients (Table 1, cases 31, 54) had severe headache, both being trial labours, of 24 and 37 hours' duration. In the second case, the section was done during a heavy barrage. The headache persisted for several days, but was relieved by pituitrin and veganin. Neither patient made any complaint when seen at the post-natal clinic 6 weeks after discharge.

A small number of patients had mild headache of a few hours' duration, generally the morning after the operation, but all yielded to veganin, and were of no real significance.

All our mothers are visited, as part of our follow-up, by health visitors, who send a written report to the Medical Officer of Health. These reports are filed in the dossiers at the clinic, and are seen by me. In no instance has there been any complaint of headache after discharge.

The incidence of severe headache must, therefore, be counted as small.

Chest complications. One patient (Table 1, case 32) had bronchitis, and one (Table 1, case 57) had pneumonia and pleurisy, with a small effusion.

Thrombophlebitis. Four patients developed this condition (Table 1, cases 24, 26, 27, 69). The first 3 were in labour 4, 4, and 6 hours respectively, and the last was a trial labour of 55 hours, the lochia of which became offensive. Case 26 was mild, the other patients were retained in hospital 4-6 weeks, and all made good recoveries.

Post-operative distension. This was rare, and when it did

occur, yielded to enemas and eserine. There were no cases of vomiting.

Secondary post-partum haemorrhage. We have had no instance of this, not even in the patients whose uteri were packed to control haemorrhage from a lower-segment placental site.

The Ages of the Patients.

The youngest patient in the series was 18 years, and the oldest was 44 years. Taking the standard of 31 years to denote "elderly primiparity," 14 patients come under this category, the oldest primipara being 43 years. It is well known that elderly primiparae are apt to be very anxious about the welfare of their babies and themselves, and that such anxiety might well militate against the state of mental tranquillity which Ashworth considers important to ensure before submitting patients to spinal anaesthesia. None of our elderly primiparae appeared to be so influenced. Five of them had trial labours, namely, Table 1, cases 3, 31, 36, 53, 57, the duration of whose labours were 85, 24, 29, 144 and 35 hours respectively, the last two being in labour during, and being operated upon during, the "blitzkrieg."

In our opinion the age of the patient need not, *per se*, be taken into consideration in weighing the pros and cons of spinal versus other methods of anaesthesia.

A Study of the Individual Tables

Table 1. It will be seen that 40 patients in this table were given trial labours of 8 hours or more, 26 of whom were in labour for more than 16 hours, and 19 were in labour for more than 24 hours. It might be thought that a trial labour of more than 24 hours might result in maternal exhaustion (which in turn might be considered a contra-indication of spinal anaesthesia). All these mothers were ensured adequate rest and relief from pain by the timely administration of omnopon gr. 1/3, with scopolamine gr. 1/150, and were given copious drinks of water or lemonade with glucose. The temperature and pulse-rate were registered hourly. As a general rule, the labour was allowed to go on, provided the maternal and foetal conditions were satisfactory, until the membranes ruptured and for about an hour after. The foetal heart-rate was registered every half-hour until the membranes ruptured, and about every 10 minutes after this. A rectal examination was made immediately the membranes ruptured, at which the degree of cervical dilatation

and the position of the vertex were noted, and to guard against the possibility of a prolapsed umbilical cord. It will be noted that 2 of the operations were performed on account of foetal distress attributable to malposition of the umbilical cord. Both these infants would undoubtedly have perished had the sections not been promptly carried out.

Vaginal examinations were not permitted in cases of trial labour. Reference has already been made to trial labours in elderly patients. In the absence of any other contra-indication, we see no reason why an elderly primipara should not be given a trial labour, but very close observation of mother and foetus is necessary, and, no doubt, earlier intervention may be called for in such patients as compared with the younger women.

Table 2. In the 20 cases of placenta praevia, 11 placentas were central and 9 were marginal. We do not subject cases of lateral placenta praevias to Caesarean section.

This is the group in which may be encountered the combination of severe anaemia and low blood-pressure, each of which is mentioned by Ashworth as a contra-indication to spinal anaesthesia. In most of our cases we have checked the blood condition by the percentage of haemoglobin, and have, when necessary, made use of blood transfusions. In 5 of our cases the transfusions were running in while the section was proceeding. Other patients were transfused preparatory to or after section. Prior to the outbreak of war, British Red Cross donors were used. Since the establishment of Blood Banks, stored blood has been used, of group O, and not more than 3 days old. We have found stored blood entirely satisfactory, and keep a small reserve in the refrigerator, so that we can begin transfusion within 5 minutes after the need arises.

This table shows the only maternal death which occurred in the series, but it is not attributable to the anaesthetic.

It is interesting to note that Marshall, in recording 43 cases of placenta praevia treated by Caesarean section, states that 14 were done under spinal anaesthesia, with no maternal or foetal deaths.

Table 3. Under this heading are included cases in which were present a combination of various conditions which decided the issue in favour of section. A few might equally well have been included under Table 1. There were 5 cases of fibroid uteri, but, as will be seen, this was not the only indication for section, other factors being age, previous obstetric history, malpresentation, and so on.

CAESAREAN SECTION UNDER SPINAL ANALGESIA

Included in this table are 2 cases of developmental abnormalities of the uterus (case 7, bicornute uterus, and case 12, uterus didelphys, who also had a placenta praevia and hypertension).

The obstetric history of case 8 is also interesting, and here again, the placenta was praevia, and adherent to the scar of the previous rupture of the lower segment. Neither case 8 nor case 12 are included in the table of placenta praevias, as the abnormal situation of the placenta was only discovered at section, which was performed for another indication.

Table 4. Both these cases of cardiac disease gave no anxiety under their spinal anaesthesia, though the disease was well established. Both were admitted for several weeks' rest and treatment before section, which no doubt contributed largely to the safe outcome.

Table 5. It will be noted that both cases 1 and 2 in this table had had previous Caesareans, the toxaemias being added com-

Table	Case No.	No. of Caesarean sections	Anaesthetic			
1	7	3	Gas and air	2	Spinal	1
	70	3	,,	2	,,	1
	14	2	,,	1	,,	1
	21	2	,,	1	,,	1
	28	2	,,	1	,,	1
	39	2	,,	1	,,	1
	52	2	,,	1	,,	1
	56	2	,,	1	,,	1
	58	2	,,	1	,,	1
	15, 16	same case 2	Both under spinal			
	18, 19	same case 2	Both under spinal			
	39, 74	same case 2	Both under spinal			
3	5, 6	same case 3	,,	1	Spinal	2
	9	2	,,	1	,,	1
	10	2	,,	1	,,	1
5	1	2	,,	1	,,	1
	2	2	,,	1	,,	1
1, 3	68, 21	same case 2	Both under spinal			

plications. In case 1 there had already been 2 small toxic accidental haemorrhages when the section was performed. Case 2 was that of a recurrent toxaemia. Case 3 was a severe toxaemia of the hepatic type.

Reference has already been made to the fact that 12 toxaemic patients were submitted to Caesarean section under spinal anaesthesia in our series. Of the 18 cases of toxaemia operated upon by Marshall, 9 (including one eclampsia) were done under spinal anaesthesia. It seems that toxaemia is not a contra-indication to spinal anaesthesia.

Repeat Caesareans

The following table shows the patients who have had 2 or more Caesarean sections, together with the type of anaesthetic. It will be seen that 5 of our patients have each had 2 Caesarean sections under spinal anaesthesia, performed by us.

The Type of Operation Performed

Of 121 Caesarean sections performed:

95 were Lower Uterine Segment Caesarean sections, 78.51 per cent.

26 were Classical Caesarean sections, 21.48 per cent.

Summary and Conclusions

A series of 121 Caesarean sections performed under spinal anaesthesia is presented, together with tables showing the indication for section, type of spinal anaesthetic used, type of section performed, and other relevant details.

Recent literature is discussed, with special reference to the advantages and dangers, indications for and contra-indications to, the use of spinal anaesthesia in advanced pregnancy. The views of various authorities as to the special susceptibility of pregnant women to the cocaine group of drugs are given. Reference is made to the multiplicity of drugs used for inducing analgesia by the spinal route, some being related to the cocaine group, others not so related.

The technique of administration, and dosage in individual cases of heavy percaine (Ciba, Ltd.), is given, and attention is drawn to the simplicity of technique in the injection of this solution into the spinal canal, and the resultant minimal disturbance of the patient.

Premedication is discussed, with special reference to the necessity to combat the fall in blood-pressure often associated with spinal anaesthesia.

Heavy percaine, hyperbaric solution, 1 : 200, with 6 per cent glucose, has been used in all our cases except 3, with no maternal mortality referable to the anaesthetic. We consider it to be a safe and suitable drug for use in spinal anaesthesia in selected cases of advanced pregnancy. It has given eminently satisfactory results as used by us in the Croydon County Borough Obstetric Service. We suggest that it is worthy of an extended trial by other obstetricians, and we feel that until this has been made, spinal anaesthesia should not be condemned.

So far as we are aware, this is the only series of Caesarean sections performed under heavy percaine which has been published. We are, therefore, unable to compare our results with those of other obstetricians using the same solution and technique.

We desire to acknowledge our indebtedness to Dr. Oscar M. Holden, Medical Officer of Health, County Borough of Croydon, for permission to publish these results, all the patients in the series having been operated upon in the two hospitals of the Croydon Obstetric Service, namely, Mayday Hospital (Maternity Department) and St. Mary's Maternity Hospital.

We also wish to pay tribute to the skill and care of our assistants in the Croydon Obstetric Service who were responsible for the administration of the spinal anaesthetics, namely, Dr. R. M. Millen, Dr. Baillie Higginson, Dr. Kenneth Seager, and Dr. S. A. Bond. The success of the anaesthesia is due to them, and they have performed a certain number of the Caesarean sections which have been recorded in the series.

Note on Case 75, Table 1.

This case was operated upon after this paper had been completed. In including it, we make this special note to record an experience in regard to variations in blood-pressure, and emotional upsets, which was quite unusual, and, in fact, the only one of its kind in the whole series. The variations in blood-pressure, the events which transpired, and the treatment adopted, are shown in the table attached. The history is as follows:

The patient had lost her first baby during a very difficult breech extraction, and had mild uterine sepsis followed by a

femoral thrombophlebitis and a rather protracted convalescence.

Her condition during the present pregnancy had been normal apart from the fact that the presentation was again a breech. She had been booked for Caesarean section at term, and an attempt at external version had not been made. She had been very cheerful and confident until the 39th week, when, for the first time, she expressed anxiety as to whether the baby would be all right. She was reassured as to this, and arrangements were made to admit her to hospital the following week, for section 2 days later. In the meantime we had 2 very severe air-raids, during the first of which the Maternity Department at Mayday Hospital was so damaged that it had to be evacuated, and the hot-water system at St. Mary's Maternity Hospital was also put out of action, making it impossible to use the theatre there. She was therefore admitted to the gynaecological ward at Mayday Hospital. She was unable to sleep without sedatives during the 2 nights preceding section, and had lost a considerable amount of sleep on account of the recent raids before admission.

On the morning of section, she received the usual premedication of ephedrine and atropine, and came to the theatre apparently cheerful. The spinal was given by the usual technique, the blood-pressure then being 135/80 Hg. After 10 minutes she vomited, the pressure having dropped to 100/58 Hg. Oxygen and carbon dioxide were administered with relief. The section was thereupon started, and progressed to the stage where the peritoneum over the lower segment was incised. At this time, she got very agitated, expressed great concern over her baby, and burst into a fit of hysterical weeping, this being co-incident with a steady further drop in blood-pressure as shown in the table. A warm pack was placed over the abdomen, and coramine 1.7 c.c. was given, and repeated with ephedrine gr. 1/2 10 minutes later, the oxygen and carbon dioxide being continued. She did not show any signs of collapse, and when she had settled down again, the uterus was opened and the child delivered. It cried at once, whereupon she had another fit of weeping, this time doubtless occasioned by the joy of hearing her baby, and her blood-pressure rose at once to 130/75 Hg. She gave us no further anxiety, though remaining a little lachrymose, and when the abdomen was closed her blood-pressure was 120/70 Hg, and her condition quite satisfactory.

The height of level of anaesthesia was found to have reached the 3rd dorsal vertebra, which is much higher than we aim at

for Caesarean section, and this was, we are sure, due to the Trendelenburg position having been slightly overdone. The influence of the emotional upsets described above, however, make it difficult to give a definite opinion as to the cause of the drop in blood-pressure, which is far greater than anything we have experienced, though, as already stated, there were no signs of collapse. Whatever influence the height of anaesthesia had on the drop in pressure must, however, be attributed to the error in technique rather than to method of anaesthesia, and is, therefore, a warning to be scrupulously careful in the degree of Trendelenburg slope adopted.

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TABLE I.—Trial Labour and Disproportion.

TABLE I.—Trial Labour and Disproportion.

Abbreviations.

H.P.—heavy percaine. L.P.—light percaine. S.B.—stillbirth. N.N.D.—neonatal death. L.—lived. D.—died. A.P.H.—antepartum haemorrhage. P.P.H.—post-partum haemorrhage. E.C.V.—External cephalic version. L.S.—lower segment. C.S.—Caesarean section. P.N.—Post-natal. I.U.—Intra-uterine glycogen. Hb.—Haemoglobin. O.P.P.—Occipito posterior position. B.P.—Blood-pressure.

Case No.	Reg. No.	Age	Grav.	Mat.	Duration of labour hours	minutes	Type of operation	Remarks
1	38/213	24	1	39	27	0	L.S.	H.P. 3 c.c.
2	37/1803	26	2	40	4	0	L.S.	L.P. 14 c.c. First baby died at 2 hours (unreduced O.P.P.)
3	37/1846	33	1	39	85	0	L.S.	H.P. 3 c.c. Precature rupture of membranes Primary inertia. Loss at op. 4 ounces.
4	38/224	22	1	40	17	30	L.S.	H.P. 2.7 c.c.
5	38/303	30	1	40	7	15	L.S.	H.P. 2.7 c.c. Contracted outlet.
6	E.In.38/228	26	2	40	19	0	L.S.	L.P. 12 c.c. Obstructed labour. Hb. 58 per cent. Previous abortion.
7	38/223	25	3	39	4	45	Class.	H.P. 2.7 c.c. Sterilized. Two previous Caesarean sections. Many adhesions encountered.
8	38/64	23	1	40	not in labour		L.S.	H.P. 2.7 c.c. Pelvic deformity. Old tubercular hip.
9	8/682	40	3	40	not in labour		L.S.	H.P. 2.7 c.c. Mild puerperal mania. Recovered. Previous N.N.D. and abortion.
10	38/1093	33	4	40	8	0	L.S.	H.P. 2.7 c.c. Two previous breech deliveries (1 S.B.) and one abortion at 28 weeks.
11	38/1120	34	1	40	not in labour		L.S.	H.P. 2.5 c.c.
12	38/1098	20	1	40	9	0	L.S.	H.P. 2.7 c.c. Premature rupture of membranes.
13	38/1350	21	1	40	31	0	L.S.	H.P. 2.7 c.c. Bougie induction. Pyrexial 7 days.
14	38/1676	22	3	39	8	30	L.S.	H.P. 2.7 c.c. Previous Caesarean section. Sterilized.
15	38/86	19	1	40	36	0	L.S.	H.P. 2.7 c.c.
16	39/1500	20	2	40	24	0	Class.	H.P. 2.7 c.c. Sterilized. The same patient. Breech presentation.
17	38/502	23	1	40	23	0	L.S.	H.P. 2.5 c.c.
18	38/IN136	29	2	40	11	0	L.S.	H.P. 2.75 c.c.
19	39/1387	30	3	40	3	0	Class.	H.P. 2.5 c.c. The same patient. First pregnancy ended as abortion. Sterilized.
20	38/2190	33	2	40	not in labour		L.S.	H.P. 2.5 c.c. Congenital syphilis. Lordosis. Previous abortion.

TABLE I.—TRIAL LABOUR AND DISPROPORTION (*continued*).

Case No.	Reg. No.	Age	Grav.	Mat.	Duration of labour hours	minutes	Type of operation	Remarks
21	38/2221	26	2	40	4	0	L.S.	H.P. 2.5 c.c. Previous Caesarean section. Ricketty dwarf.
22	38/2417	18	1	40	33	0	L.S.	H.P. 2.5 c.c. Offensive lochia. Pyrexia. I-U glyc.
23	39/12	24	2	40	8	0	L.S.	H.P. 2.5 c.c. Epileptiform attack during operation. O_2 and CO_2. Baby asphyxiated; lobeline into cord.
24	39/57	43	1	37	4	0	L.S.	H.P. 2.5 c.c. Premature rupture of membranes. Breech. Contracted outlet. Elderly primipara. Pelvic thrombophlebitis.
25	39/91	30	2	40	4	0	Class.	H.P. 2.5 c.c. Previous child died, tentorial tear.
26	39/300	31	3	40	4	0	L.S.	H.P. 2.5 c.c. Two previous abortions. Thrombophlebitis, legs (mild).
27	39/395	24	1	40	6	0	L.S.	H.P. 2.5 c.c. Previous fracture of sacrum. Thrombophlebitis, leg. Notified pyrexia.
28	39/406	33	3	40	5	0	Class. Sterilized	H.P. 2.5 c.c. Previous Caesarean for disproportion. Many adhesions between uterus and abdominal wall encountered
29	39/549	24	2	40	3	0	L.S.	H.P. 2.5 c.c. Previous abortion.
30	39/610	35	2	40	not in labour		L.S.	H.P. 2.5 c.c.
31	39/IN670	34	1	40	24	0	L.S.	H.P. 2.5 c.c. Headache for several days, relieved by pituitrin. No complaint at P-N examination (6 weeks).
32	39/IN734	27	1	40	36	0	L.S.	H.P. 2.5 c.c. Mild post-operative bronchitis. Pyrexia 3 days.
33	39/1089	25	1	40	12	0	L.S.	H.P. 2.5 c.c. Toxaemia also. B.P. 150/110. Oedema feet and legs.
34	39/750	24	2	40	not in labour		L.S.	H.P. 2.5 c.c. Previous S.B. Toxaemia this pregnancy, poor U.C.T. Blood urea, 63 mgm. per 100 c.c.
35	38/1991	21	1	40	10	0	L.S.	H.P. 2.5 c.c. Funnel pelvis. Very small outlet.
36	39/1209	32	1	40	29	0	Class.	H.P. 2.5 c.c. Uterus dextro-rotated. Fibroid excised from anterior wall. Large right broad ligament fibroid not interfered with.
37	39/1311	22	1	40	12	0	L.S.	H.P. 2.5 c.c. Membranes ruptured at commencement of labour.
38	38/1345	27	2	40	19	0	L.S.	H.P. 2.5 c.c. Previous abortion.

TABLE I.—TRIAL LABOUR AND DISPROPORTION (*continued*).

Case No.	Reg. No.	Age	Grav.	Mat.	Duration of labour hours	minutes	Type of operation	Remarks
39	39/1487	29	3	40	not in labour		L.S.	H.P. 2.0 c.c. Previous trial labour and Caesarean section. Previous abortion.
40	39/1103	27	2	40	not in labour		L.S.	H.P. 2.5 c.c. First child S,B. 10 pounds.
41	38/2105	28	1	38	19	0	L.S.	H.P. 3.0 c.c. Rigid cervix. One-third dilated after strong pains.
42	39/901	36	2	40	not in labour		L.S.	H.P. 2.5 c.c. Premature rupture of membranes. Free loss at operation. Blood transfusion 2 pints. Previous baby 12 years before, died on third day (2½ pounds).
43	39/1173	36	5	40	not in labour		L.S.	H.P. 2.5 c.c. Preceding labour impacted brow. S.B. 8 pounds. Biggest previous child, 6 pounds 5 ounces.
44	39/1233	23	1	40	12	0	L.S.	H.P. 2.5 c.c.
45	39/1269	34	2	40	not in labour		L.S.	H.P. 2.5 c.c. Previous labour failed forceps and craniotomy, with subsequent paresis of leg.
46	39/1541	22	1	40	not in labour		L.S.	H.P. 2.5 c.c. Persistent malpresentation.
47	39/1549	25	1	40	32	0	L.S.	H.P. 2.5 c.c.
48	39/1596	35	2	40	3	0	L.S.	H.P. 2.5 c.c. Previous Caesarean section for disproportion.
49	39/1696	26	1	40	vague pains		L.S.	H.P. 2.5 c.c. Free bleeding after expression of placenta.
50	37/1451	29	1	40	11	0	L.S.	H.P. 2.5 c.c.
51	37/1706	29	2	40	not in labour		L.S.	H.P. 2.5 c.c.
52	40/473	27	2	40	5	0	Class.	H.P. 2.5 c.c. Previous Caesarean section. Small bowel adherent to abdominal incision. Sterilized. B.P. before section 136/ 92.
53	40/588	34	1	40	144	0	L.S.	H.P. 2.5 c.c. Membranes ruptured 7 days before section. Uterine inertia. Soluseptasine 20 c.c. before section, pyrexial 1 day.
54	40/520	21	1	40	37	0	L.S.	H.P. 2.5 c.c. Membranes ruptured 48 hours. Soluseptasine 20 c.c. before section. Low grade uterine and wound sepsis. Frontal headache 4 days, relieved by pituitrin 0.5 c.c. b.d. Discharged well on 23rd day.
55	40/579	28	1	40	17	0	L.S.	H.P. 2.5 c.c. Ricketty dwarf with deformed pelvis. Foetal distress and apnoea. Lobeline into cord. Recovery.

TABLE I.—TRIAL LABOUR AND DISPROPORTION (*continued*).

Case No.	Reg. No.	Age	Grav.	Mat.	Duration of labour hours	minutes	Type of operation	Remarks
56	40/504	32	2	39	4	0	L.S.	H.P. 2.5 c.c. Prolapsed cord and foetal distress. Previous Caesarean for pelvic contraction. Many adhesions found.
57	40/289	35	1	40	35	0	L.S.	H.P. 2.5 c.c. Developed basal pneumonia and small effusion during puerperium. Good recovery.
58	40/241	28	2	40	6	0	L.S.	H.P. 2.5 c.c. Previous Caesarean section. Hypertension also. B.P. 148/90. Sterilized.
59	40/187	31	3	40	not in labour		L.S.	H.P. 2.5 c.c. Previous S.B. failed forceps and craniotomy, and abortion.
60	40/141	23	1	40	8	0	L.S.	H.P. 2.5 c.c. Small pelvis. Breech with extended legs.
61	40/208	26	1	40	9	0	Class.	H.P. 2.5 c.c. Small outlet. Breech with extended legs.
62	40/788	37	2	40	31	0	L.S.	H.P. 2.5 c.c. Previous child 14 years before.
63	39/1669	25	1	40	48	0	Class.	H.P. 2.5 c.c. Foetal distress with vertex still above brim. Cord found tight round child.
64	38/IN906	22	1	40	24	0	L.S.	H.P. 2.5 c.c.
65	38/1880	25	1	40	not in labour		L.S.	H.P. 2.5 c.c. Dextro-cardia. Premature rupture of membranes. Vertex floating.
66	39/832	26	1	40	96	0	L.S.	H.P. 2.5 c.c. Posterior position of vertex. Very irregular contractions. Maternal distress. Offensive lochia and pyrexia. Good recovery.
67	40/802	36	3	40	96	0	L.S.	H.P. 2.5 c.c. Membranes ruptured 4 days. Pyrexia one day. Good recovery.
68	39/IN457	30	2	40	10	0	L.S.	H.P. 2.5 c.c. Complex presentation (vertex, hand and foot.)
69	39/952	21	1	40	55	0	L.S.	H.P. 2.5 c.c. Offensive lochia. Thrombophlebitis, leg. Discharged in 5½ weeks.
70	39/953	33	4	40	not in labour		L.S.	H.P. 2.5 c.c. Two previous Caesarean sections. Toxaemia also. B.P. 122/92. Oedema. Sterilized.
71	37/1563	20	1	40	7	0	L.S.	H.P. 2.5 c.c.
72	41/IN85	21	1	40	12	0	L.S.	H.P. 2.5 c.c. Membranes ruptured before labour.
73	41/288	23	1	40	18	30	L.S.	H.P. 2.5 c.c. Vertex in right iliac fossa after 18 hours' labour.
74	41/264	30	3	40	not in labour		L.S.	H.P. 2.5 c.c. Two previous Caesarean sections. Same case as Table 1, case 39. Sterilized. See B.P. record p. 261.
75	41/471	29	2	40	not in labour		L.S.	H.P. 2.5 c.c. Previous S.B. See special note at end of paper.

TABLE II.—PLACENTA PRAEVIA.

TABLE II.—PLACENTA PRAEVIA.

Case No.	Reg. No.	Age	Grav.	Mat.	Amount of A.P.H.	Situation of placenta	Loss at operation	Type of operation	Remarks
1	38/140	32	4	36	20 ounces	Marginal	40 ounces	Class.	H.P. 2.7 c.c. Pyrexial. Hb. after section, 59 per cent.
2	38/349	29	6	38	Two shows and 10 ounces	Central	40 ounces on table before section	Class.	H.P. 2.7 c.c. Blood transfusion 50 ounces during section. No previous live child. Hb. week after section, 78 per cent.
3	38/IN439	23	1	40	Small	Marginal	Very little	L.S.	H.P. 2.5 c.c. Hb. 63 per cent. Disproportion also.
4	38/IN2a	37	6	36	20 ounces	Central	Very little	Class.	H.P. 2.5 c.c. Blood transfusion 25 ounces during section. Hb. after section 60 per cent.
5	38/1160	27	2	39	Two shows	Central	Small	L.S.	H.P. 2.5 c.c. Old tubercular hip (7 operations). Sterilized.
6	38/IN839	18	1	38	None	Marginal	Small	Class.	H.P. 2.5 c.c. Placenta praevia revealed at exam. for non-engagement of vertex.
7	38/1130	26	2	39	Several small losses	Marginal	Small	L.S.	H.P. 2.5 c.c.
8	38/1629	28	2	39	Several losses	Marginal	20 ounces	L.S.	H.P. 2.5 c.c. Hb. before section 82 per cent. Infant died same day.
9	39/426	23	1	40	None	Marginal	Small	Class.	H.P. 2.5 c.c. Persistent transverse, recurred after two versions. Examination under spinal. Pelvic capacity ample.
10	39/IN736	25	1	40	Several small and one severe	Central	10 ounces	Class.	H.P. 2.5 c.c. Hb. before section 42 per cent. Blood transfusion 40 ounces during section.
11	38/221	29	3	38	Several small and one severe	Central	Very little	L.S.	H.P. 2.5 c.c. Hb. before section 53 per cent. Blood transfusion 25 ounces during section. Hb. on discharge 75 per cent.
12	40/465	38	1	39	None	Central and posterior	Very little	L.S.	H.P. 2.5 c.c. Persistent malpresentation. Three E.C.V's for breech and transverse lies. Examined under spinal for suspected placenta praevia.

TABLE II.—PLACENTA PRAEVIA (*continued*).

Case No.	Reg. No.	Age	Grav.	Mat.	Amount of A.P.H.	Situation of placenta	Loss at operation	Type of operation	Remarks
13	41/384	38	2	36	Several shows one heavy	Central	Slight	L.S.	H.P. 2.5 c.c. Hb. before section 54 per cent. Blood transfusion.
14	40/IN646	28	1	38	Several small losses	Marginal and posterior	8 ounces	L.S.	H.P. 2.0 c.c. Hb. before section 74 per cent. Examination under spinal, followed by section.
15	40/IN471	20	2	36	Several moderate losses	Central	Slight	Class.	H.P. 2.5 c.c. Hb. before section 65 per cent. Blood transfusion during section of 40 ounces. Hb. after section 75 per cent.
16	39/442	36	3	40	20 ounces	Central	Slight	Class.	H.P. 2.5 c.c. Pulmonary embolism 9th day. P.M. showed small clot in popliteal vein. Death not attributable to anaesthetic.
17	41/IN194	35	5	36	Several shows, and two of 8 ounces each	Central	Slight	L.S.	H.P. 2.5 c.c. Vertex in right iliac fossa. Hb. after section 61 per cent. Blood transfusion of 40 ounces immediately after section.
18	41/397	24	1	40	None	Central	20 ounces uterus packed	L.S.	H.P. 2.5 c.c. Persistent transverse lie during pregnancy. Three attempts at version failed. Blood transfusion of 40 ounces immediately after section.
19	41/IN196	37	7	38	Severe loss at 28th week. Hb. after 1 pint of blood transfusion, 46 %	Marginal and posterior	16 ounces	L.S.	H.P. 2.5 c.c. Blood transfusion of 90 ounces, including 36 ounces concentrated cells. Hb. rose to 74 per cent. Treatment with iron for 10 days. Hb. after section 76 per cent.
20	41/257	22	1	40	Slight show	Marginal and posterior	8 ounces	L.S.	H.P. 2.5 c.c. Admitted to hospital before show occurred, as suspected placenta praevia.

TABLE III. MISCELLANEOUS.

Case No.	Reg. No.	Age	Grav.	Mat.	Duration of labour	Type of operation	Indication for operation	Remarks
1	38/708	39	1	40	Not in labour	Class. Myomectomy	Elderly primipara. Fibroid uterus. Breech with extended legs.	H.P. 2.7 c.c.
2	38/318	26	1	40	Not in labour	Class. Sterilized	Severe myopia. Contracted outlet. Breech.	H.P. 2.7 c.c.
3	38/850	39	2	40	4 hours	L.S.	Fibroid uterus. First baby S.B.	H.P. 2.7 c.c.
4	38/1206	31	1	38	44 hours	Class.	Rigid cervix. Foetal distress.	H.P. 2.7 c.c.
5	38/602	23	2	40	Not in labour	L.S.	Previous L.S. Caesarean for placenta praevia. This pregnancy—large child. Breech presentation.	H.P. 2.7 c.c.
6	40/195	24	3	40	Not in labour	L.S.	See above. Two previous L.S. Caesareans. Third pregnancy—very large child. Previous lower segment scars seen to be sound at succeeding operation.	H.P. 2.5 c.c. The same patient.
7	38/1664	21	1	40	Not in labour	L.S.	Bi-cornute uterus. Persistent malpresentation. Breech at operation.	H.P. 2.7 c.c.
8	38/1932	30	3	40	Not in labour.	L.S. Sterilized	Bad obstetric history: 2 previous manual removals for P.P.H., forceps delivery in 2nd labour, with ruptured lower segment, and puerperal sepsis on each occasion. At section, placenta adherent to scar in lower segment. Uterus packed to control haemorrhage.	H.P. 2.7 c.c.
9	38/1343	24	3	40	5 hours	L.S. Sterilized	Previous L.S. Caesarean for placenta praevia. Persistent malpresentation in this pregnancy.	H.P. 2.7 c.c.
10	38/2124	25	2	40	5 hours	Class. Sterilized	Previous L.S. Caesarean for disproportion.	H.P. 2.7 c.c.
11	37/1783	28	1	39	72 hours	Class.	Twins. Premature rupture of membranes. Foetal distress and meconium-stained liquor when one-fifth dilated.	

TABLE III. MISCELLANEOUS (*continued*).

Case No.	Reg. No.	Age	Grav.	Mat.	Duration of labour	Type of operation	Indication for operation	Remarks
12	40/161	31	1	40	Not in labour	Class.	Uterus didelphys. Pregnancy in left uterus. Hypertension also. B.P. 144/100. Placenta in lower segment.	H.P. 2.5 c.c.
13	40/613	39	1	40	Not in labour	L.S.	Elderly primipara. Small pelvis. Breech with extended legs.	H.P. 2.5 c.c.
14	40/759	43	4	40	Not in labour	Class. Sterilized	Bad obstetric history. Hypertension B.P. 170/90. Twins.	H.P. 2.5 c.c.
15	39/73	28	1	40	22 hours	L.S.	Obstructed labour. Post-cervical fibroid.	H.P. 2.5 c.c.
16	38/2196	29	1	40	Not in labour	Class.	Fundal and cervical fibroids. Hypertension. B.P. 150/90.	H.P. 2.5 c.c.
17	38/1357	37	1	40	84 hours	L.S.	Uterine inertia. Rigid cervix. Foetal distress. Note: uterine and wound sepsis. One continuous and 12 interrupted catgut sutures passed p.v. Incision finally healed well.	Stovaine 1.8 c.c.
18	40/1350	44	2	40	4 hours	L.S.	Fibroid uterus. Persistent malpresentation. First child died at one day from cerebral injury—forceps delivery.	H.P. 2.5 c.c.
19	41/510	32	1	40	Not in labour	L.S.	Congenital dislocation of hip. Several inches shortening of leg, with gross pelvic deformity.	H.P. 2.5 c.c.
20	41/584	20	1	40	18 hours	L.S. Ovariotomy	Obstructed labour. Ovarian dermoid cyst size of foetal head.	H.P. 2.5 c.c.
21	41/145	31	3	40	Not in labour	L.S. Sterilized	Previous Caesarean for complicated presentation. See Table 1, case 68. Persistent transverse lie in this pregnancy. 4 E.C.Vs.	H.P. 2.5 c.c.

TABLE IV.—Cardiac Disease.

Case No.	Reg. No.	Age.	Grav.	Mat.	Cardiac condition	Type of operation	Remarks
1	38/1596	38	3	39	Post-rheumatic aortic and mitral disease. Compensation good. Four weeks' rest in hospital before operation.	L.S. Sterilized	Coramine before, and oxygen throughout operation. H.P. 2.5 c.c.
2	39/1014	24	4	36	Mitral stenosis. Several attacks of dyspnoea and cyanosis. Several weeks' rest in hospital before operation.	L.S. Sterilized	H.P. 2.5 c.c.

TABLE V.—Toxaemia.

No. Case	No. Reg.	Age	Grav.	Mat.	Highest B.P.	Other signs	Type of operation	Remarks
1	39/55	34	2	38	174/98	Oedema. Albuminuria 0.4 per cent. Accidental haem.	L.S.	H.P. 2.5 c.c. Previous classical Caesarean section. Multiple adhesions encountered. Space for L.S. cleared by dissection. Two retroplacental clots found.
2	39/319	34	2	40	164/118	Albuminuria. Previous toxaemia. Contracted pelvis. Previous Caesarean.	L.S.	H.P. 2.5 c.c.
3	39/IN369	30	1	38	——	Jaundice, vomiting, epigastric pain. Van den Bergh test—indirect positive.	L.S.	H.P. 2.5 c.c. B.P. on discharge 130/84. Jaundice cleared.

The Macrocytic Anaemia of Pregnancy *

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THIS paper deals mainly with the macrocytic type of anaemia occurring in pregnancy. In recent times, the severe forms of anaemia met with in the tropics have received much attention and numerous attempts have been made to arrive at a conclusion regarding their aetiology and treatment. While some success has resulted in cases occurring in men, the reports on the anaemias met with in pregnancy are still varied and contradictory. Our attempt to arrive at some conclusions as regards the aetiology and treatment of the anaemias in pregnancy is set forth below.

We have in this paper taken into consideration only the macrocytic anaemias met with in pregnancy. The ordinary microcytic hypochronic anaemia is very common in Madras and we have not considered it in any detail in this paper. The diagnosis of macrocytic anaemia was made after examination of blood smears, determining the mean cell volume, estimation of haemoglobin, red and white cells and reticulocytes. This series deals with 103 cases of macrocytic anaemia of which 16 cases were complicated with ankylostomiasis.

The macrocytic anaemia of pregnancy, often called the pernicious anaemia of pregnancy, is a severe form of anaemia which occurs in the pregnant woman, manifesting itself more often in the later months of pregnancy. While this disease seems to be

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somewhat rare in European countries, it is much more frequent in India and other tropical countries.

As early as 1915 the incidence of this disease was reported by one of us (Mudaliar[1]). In recent times the disease has been studied and discussed by Balfour[2], Macsweeney[3], Mitra[4, 5], Wills[6], Mudaliar and Rao[7] and Napier[8]. It has now attracted the attention of those obstetricians and general physicians who are interested in maternity and child welfare, particularly in tropical countries.

Incidence. It is difficult to arrive at a correct conclusion regarding the incidence of macrocytic anaemia. According to European and American standards, any pregnant woman with a haemoglobin of less than 80 per cent, and 4 million red blood cells, is considered anaemic. We estimated the haemoglobin and red blood cells in 300 consecutive patients attending the Antenatal Clinic, in the 2nd and 3rd trimesters of pregnancy. These 300 pregnant women were not suffering from any complications and were apparently normal in health. It was found that the average haemoglobin index in the series was 66 per cent and red blood corpuscles 3.8 millions. If Western standards had been applied to this series, only 28 cases would not have been classed anaemic. Only 10 had haemoglobin 80 per cent or above, while 18 per cent had a haemoglobin between 70 and 80 per cent. It is clear that one cannot proceed on the standards laid down in the West. We have, therefore, included in this series only patients with a haemoglobin index less than 60 per cent.

These 103 cases of macrocytic anaemia were among 1,200 patients admitted into the antenatal wards for various complications, thus forming 8.6 per cent of all complications in pregnancy. In the United States of America (Ordway[9]) the incidence varies from 1 in 6,000 to 1 in 10,000 and it is supposed to be rare in England (Osler[10], Evans[11]). In Madras, however, it appears to be as common as pre-eclamptic toxaemia—especially in recent years such cases are more frequent, perhaps due to the larger number of patients who attend the antenatal clinic and more thorough haematological studies and better appreciation of the nature of the disease.

Distribution According to Race and Caste

The table below gives the distribution according to race and caste:

TABLE I.

Caste	Hindu	Muhammadan	Indian Christian	Anglo-Indians	Total
No. of cases	76	7	14	6	103

With this distribution the factor of vegetarian and non-vegetarian diet has to be considered. Hindu women in this group were both vegetarians and non-vegetarians. It would appear that the anaemia is prevalent almost equally in both classes—52 per cent of vegetarians and 48 per cent of non-vegetarians. The apparent low incidence of the anaemia among Muhammadans is perhaps due to the smaller number of Muhammadan women seeking admission to the hospital and that in the Anglo-Indian due to the appreciation of antenatal care in pregnancy and attendance at efficient clinics from early months of pregnancy.

DISTRIBUTION ACCORDING TO AGE

The table below gives the distribution according to age:

TABLE II.

	15 to 20 years	20 to 30 years	30 to 35 years	35 to 40 years	Total
Cases	23	58	18	4	103
Percentage	22.3	56.3	17.4	3.8	

The maximal number of cases occur in patients between 20 and 30 years of age.

DISTRIBUTION ACCORDING TO PARITY

The table below shows the relation of anaemia to parity:

TABLE III.

Parity	1	2	3	4	5	6	7	8	9	10	11	12	Total
Cases	25	15	18	17	7	11	3	3	2	1	—	1	103

Percentage:

Primipara, 24.2 per cent. Multipara, 75.8 per cent.

Mitra[5] observes the greater incidence in primigravidae as also Choudry and Mangalik[12]. We, however, find that in Madras it is more common in multiparae.

Distribution According to the Period of Pregnancy

The following table shows the period of pregnancy in relation to the anaemia.

Table IV.

	20 to 28 weeks	28 to 32 weeks	32 to 40 weeks	Total
Cases	27	62	14	103
Percentage	26.2	60.2	13.6	

It is clear that most of the patients come under observation during the second and third trimesters.

Monthly Distribution of Cases

Wills[6] observes that the disease appears to be seasonal in Bombay, most of the cases occurring between October and March. We give below the monthly incidence of the disease in this series:

Table V.

Month	No. of cases	Month	No. of cases
January	7	August	7
February	10	September	14
March	5	October	12
April	5	November	14
May	5	December	12
June	7		
July	5	Total	103

The maximal number of patients have been admitted in September and October, while November and December follow closely. The cases became fewer with the onset of the summer. While it is difficult to come to a definite conclusion regarding the epidemology it must be borne in mind that in this hospital we have the maximal number of admissions and confinements in the September to December period.

Clinical History

Little advance has been made in the description of these cases and there is not much to add to the clinical description given 25 years ago (Mudaliar). The disease has an insidious onset and is more frequent in multiparae than in primigravidae. Patients hardly realize the gravity of the condition till the whole body is

swollen or they are subject to attacks of dyspnoea on the slightest exertion. The woman is usually in the 2nd or 3rd trimester of pregnancy and occasionally one obtains the history of such anaemia in previous pregnancies. The clinical picture is characteristic—the oedematous patient with that particular lemon yellow tint most marked in those of fair complexion, the hurried dyspnoeic breathing, the pulsating jugulars, the white sclerotics with a suspicion of a yellowish tinge of the conjunctiva, the pale occasionally sore tongue, the extraordinary pallor of the nails and lips—all these constitute a picture which once seen can never be forgotten.

Symptoms

The commonest symptoms for which the patients come into hospital are (1) oedema, (2) dyspnoea, (3) diarrhoea, (4) heartburn, nausea, vomiting. Any one or combination of these may be present.

Oedema. This we believe is the commonest symptom. It occurred in 82 per cent of our patients. It is of varying grades. Seventy per cent of the patients had severe degree of oedema involving extremities, face, abdominal wall, the labia and in 2 cases ascites also. In 18 per cent of the cases oedema was absent. The oedema is of the soft pitting type and clears up quickly under treatment.

Dyspnoea. This is the next common symptom. Sixty per cent of the patients came in complaining of dyspnoea. While in 16 per cent the dyspnoea was so severe as to be present even while the patients were at rest, in the remainder it came on with the slightest exertion. Dyspnoea in conjunction with oedema account for the majority of these patients coming into hospital.

Diarrhoea. In the tropics, diarrhoea in pregnancy is a common complaint. We believe from what we have observed that in many cases the diarrhoea is a precursor of the macrocytic anaemia of pregnancy. Twenty-two per cent of our patients were admitted for diarrhoea only. On questioning carefully the remainder, we were able to gather that 30 per cent of them had diarrhoea lasting for a month or more at some time during pregnancy. It is, perhaps, not incorrect to assume that the diarrhoea may have caused some derangement of the absorption and utilization of the anti-anaemic principle, the deficiency or deficient utilization of which led to the macrocytic anaemia. Astringents are seldom necessary to stop the diarrhoea; they clear up with injections of liver extract.

Other symptoms. Many patients complain of nausea, vomiting and vague ill-health—but most of them seek admission for the other complaints stated above. Especially in the early cases, nausea and heart-burn are common symptoms.

Physical signs. The patient is very weak, dyspnoeic, presents a fairly lemon yellow colour. "It is neither the muddy complexion of ankylostomiasis nor the sallow complexion of malaria but has a distinct feature by itself" (Mudaliar and Rao). The face is puffy, in severe cases the patient is unable to open her eyes and there is oedema of different grades. Albumin was present in traces in 10 per cent of cases while in those cases complicated with ankylostomiasis it was present to a severe degree. The blood-pressure is usually normal or below normal in a few patients except in those cases complicated with ankylostomiasis where it was high ranging from 160 mm. of mercury to 200 mm. systolic. The heart is in almost all cases dilated to a moderate extent. Haemic murmurs are almost always present and the heart sounds soft. Congestion of the lungs is not uncommon, the pulse-rate is rapid—average 110. The spleen and liver were not palpable in any one of our series.

The disease takes a progressive course until interrupted by death or treatment or spontaneous improvement occurs after confinement. "Labour generally sets in prematurely and is precipitate; the patient getting into much worse condition after parturition. In fact, this period seems to be much more critical as with the birth of the child the breathing becomes more laboured, and dyspnoea sets in, the patient goes into a comatose condition and although the heart may continue to beat the respiration becomes more shallow and occurs at larger intervals till the patient expires. If the patient survives the shock of labour, the prognosis is slightly better but the first days of puerperium are still critical days and the slightest indiscretion on the part of the patient leads to a repetition of the above state of symptoms" (Mudaliar). During labour there is often a blood crisis characterized by an increase in the number of megaloblasts, normoblasts, reticulocytes and myelocytes in the blood and associated with cyanosis, dyspnoea and rapid pulse.

Haematological findings. In the majority of cases the blood investigation reveals a macrocytic hyperchromic anaemia; but there are 33 cases in our series of macrocytic hyperchromic anaemia. Table VI shows the haemoglobin percentage, in grams per cent, red and white cell counts, the colour index, the volume index, mean cell volume (M.C.V.).

TABLE VI.

No.	Haemo-globin, per cent	Haemo-globin, in grams	R.B.C., in millions	W.B.C.	Colour index	Volume index	Mean cell volume, M.C.V. =89 $c\mu$
1.	45	7.2	2.12	5000	1.1	1.5	132.0
2.	15	2.4	1.2	6300	0.8	1.1	91.6
3.	48	7.6	1.3	3750	1.8	1.4	123.0
4.	35	5.6	2.0	3125	0.8	1.02	90.0
5.	55	8.8	2.5	3750	1.1	1.5	140.0
6.	52	8.4	2.2	4375	1.1	1.5	149.0
7.	10	1.6	1.15	4375	0.5	0.9	86.8
8.	21	3.4	0.82	3125	1.2	2.2	195.1
9.	12	2.0	1.2	4375	0.5	1.2	100.0
10.	25	4.0	1.45	5000	0.8	1.2	107.0
11.	<10	—	0.75	4375	—	1.5	133.3
12.	42	6.8	1.5	3125	1.4	1.06	93.3
13.	20	3.2	1.0	5000	1.0	1.5	140.0
14.	10	1.6	0.55	4375	0.9	1.3	125.4
15.	10	1.6	0.7	5000	0.7	1.6	142.8
16.	32	5.0	1.2	3125	1.3	1.1	125.0
17.	<10	—	2.5	5625	—	1.0	95.0
18.	<10	—	0.9	4375	—	1.1	111.1
19.	22	3.6	1.14	5000	1.0	1.1	96.5
20.	38	6.0	1.18	3125	1.6	1.4	127.5
21.	30	4.8	1.5	6250	1.0	1.3	120.0
22.	30	4.8	1.1	6250	1.4	1.2	119.0
23.	<10	—	0.6	3125	—	1.5	114.3
24.	25	4.0	1.24	5000	1.0	1.4	126.0
25.	11	1.8	0.5	4375	1.1	1.3	120.0
26.	10	1.6	0.9	5625	0.6	1.2	112.0
27.	12	2.0	0.5	4375	1.2	1.2	110.0
28.	20	3.2	1.3	6250	0.8	1.1	95.0
29.	31	5.0	1.21	5000	1.2	1.8	166.3
30.	31	5.0	1.33	4375	1.2	1.2	98.6
31.	10	1.6	1.3	3125	0.5	1.2	107.7
32.	22	3.6	1.1	5625	1.0	1.1	100.0
33.	26	4.2	1.75	5000	0.7	1.3	115.6
34.	21	3.4	0.75	4375	1.4	1.3	120.6
35.	23	3.6	1.3	4375	0.9	1.3	112.6
36.	18	2.8	0.9	5625	1.0	1.1	92.0
37.	19	3.0	0.85	6250	1.1	1.1	94.5
38.	23	3.6	0.7	4375	1.1	1.3	128.0
39.	53	8.4	2.56	5000	1.1	1.2	120.0
40.	25	4.0	0.75	3750	1.6	1.3	110.0
41.	30	4.8	1.65	4375	0.9	1.2	108.0
42.	10	1.6	1.09	5625	0.5	1.1	92.0
43.	24	3.8	1.0	3750	1.2	1.8	160.0
44.	24	3.8	2.25	5625	0.5	1.2	96.0
45.	10	1.6	1.0	5625	0.5	1.2	94.0
46.	10	1.6	0.8	3750	0.6	1.2	94.0
47.	26	4.2	1.25	4375	1.1	1.3	110.0
48.	30	4.8	1.15	3750	1.3	1.3	111.0
49.	28	4.4	1.25	4375	1.1	1.3	98.0

TABLE VI (*continued*)

No.	Haemoglobin, per cent	Haemoglobin, in grams	R.B.C., in millions	W.B.C.	Colour index	Volume index	Mean cell volume, M.C.V. =89 cμ
50.	10	1.6	1.1	5625	0.5	1.1	94.0
51.	15	2.4	0.63	3750	1.2	1.3	114.0
52.	25	4.0	1.1	4375	1.1	1.3	112.0
53.	25	4.0	1.66	4375	0.7	1.2	97.0
54.	50	8.0	1.84	5625	1.3	1.2	97.8
55.	24	3.8	1.0	5625	1.2	1.2	112.8
56.	42	6.8	2.0	3750	1.1	1.1	96.0
57.	26	4.2	1.5	4375	0.8	1.1	90.0
58.	32	5.1	1.5	4375	1.1	1.5	100.0
59.	37	5.9	1.15	5625	1.2	1.5	100.0
60.	17	2.8	1.0	3750	0.8	1.1	94.0
61.	25	4.0	1.0	4375	1.2	1.2	111.0
62.	28	4.6	1.4	5000	1.0	1.2	93.0
63.	24	3.8	1.1	4375	1.1	1.1	90.0
64.	32	5.2	1.2	5625	1.3	1.3	111.0
65.	12	2.0	0.8	4375	0.8	1.2	95.0
66.	10	1.6	0.5	4315	0.5	1.2	112.0
67.	30	4.8	1.2	5000	1.2	1.2	100.0
68.	10	1.6	0.6	5625	0.8	1.1	95.0
69.	25	4.0	1.2	3125	1.1	1.3	112.0
70.	20	3.2	0.8	4375	1.2	1.3	115.0
71.	18	2.8	0.6	3125	1.5	1.3	115.0
72.	38	6.0	1.5	4375	1.3	1.2	100.0
73.	36	5.8	1.5	5625	1.2	1.2	95.0
74.	18	2.8	1.6	4375	1.5	1.3	110.0
75.	15	2.4	0.6	4375	1.2	1.2	111.0
76.	22	3.6	1:1	3125	1.0	1.2	98.0
77.	26	4.2	1.2	5000	1.1	1.1	96.0
78.	25	4.0	1.2	4375	1.3	1.3	110.0
79.	35	5.6	1.5	4375	1.2	1.2	100.0
80.	21	3.4	1.0	3750	1.05	1.1	98.0
81.	26	4.2	1.2	3125	1.05	1.1	100.0
82.	32	5.2	1.4	5000	1.1	1.2	110.0
83.	18	2.8	0.8	4375	1.1	1.2	104.0
84.	21	3.4	0.9	4375	1.2	1.2	100.0
85.	28	4.6	1.2	6250	1.2	1.3	112.0
86.	36	5.8	1.5	3750	1.2	1.1	96.0
87.	22	3.6	1.0	5000	1.1	1.3	115.0
88.	10	1.6	0.5	6250	1.0	1.4	120.0
89.	25	4.0	1.2	3750	1.1	1.3	114.0
90.	12	2.0	1.0	3750	0.6	1.2	100.0
91.	10	1.6	1.0	6250	0.5	1.1	98.0
92.	15	2.4	0.8	4375	0.9	1.2	100.0
93.	22	3.6	1.0	5000	1.1	1.2	104.0
94.	18	2.8	0.8	3750	1.2	1.3	112.0
95.	21	3.4	1.0	4375	1.1	1.2	98.0
96.	16	2.6	1.2	4375	0.7	1.3	106.0
97.	24	3.8	1.2	5000	1.0	1.3	114.0
98.	12	2.0	0.5	3750	1.2	1.2	99.0

TABLE VI (*continued*)

No.	Haemoglobin, per cent	Haemoglobin, in grams	R.B.C., in millions	W.B.C.	Colour index	Volume index	Mean cell volume, M.C.V. =89 cμ
99.	10	1.6	1.0	6250	0.5	1.3	115.0
100.	14	2.2	0.8	4375	0.9	1.2	100.0
101.	24	3.8	1.15	5000	1.1	1.2	96.0
102.	20	3.2	0.8	5000	1.3	1.2	103.0
103.	16	2.6	0.5	3750	1.6	1.3	111.0

The haemoglobin percentage varied from less than 10 per cent to 55 per cent. The group distribution is shown below.

TABLE VII.

Percentage	<10	10 to 20	20 to 30	30 to 40	40 to 50	50 to 55	
No. of cases	4	38	42	12	5	2	103

The red blood cells are markedly reduced in number sometimes as low as half a million. Their group distribution is shown below.

TABLE VIII.

R.B.C.	0.5 million	0.5 to 1 million	1 million	1 to 2 millions	Above 2 millions	
No. of cases	7	25	15	50	6	103

The white cells count showed a leucopenia throughout.

The colour index. Out of 103 cases the colour index was below 1 in 33 cases, 1 in 8 cases and above 1 in 62. Of the 33 hypochromic cases, 16 were complicated with ankylostomiasis. We observe that whenever ankylostomiasis complicates pregnancy in a woman with macrocytic anaemia, the anaemia is always of the hypochromic type and the patient in addition shows signs of toxaemia such as raised blood-pressure and severe albuminuria. We shall deal with this in detail at a later stage. According to the colour index, therefore, the cases are divided into

Macrocytic hyperchromic ... 62 cases.
Macrocytic orthochromic ... 8 cases.
Macrocytic hypochromic ... 33 cases.

Mitra makes a reference to the large number of macrocytic hypochromic type in his series. The Editor of the *Indian Medical Gazette* commenting on this remarked that if the mean cell volumes had been determined in those cases instead of depending on the halometer reading, the number of macrocytic hypochromic cases would have been much less, perhaps nil, as macrocytic and hypochromic is an abnormal combination. We have determined the mean cell volume in all cases and we find that such types are not at all uncommon—in fact we may say they are quite common.

The mean cell volume and mean cell haemoglobin. These were characteristically high in this series. Mean cell volume ranges from 86.8 cμ to 160 cμ. If we take 85 cμ as the normal all our cases then belong to the typical macrocytic group. The mean cell haemoglobin was above the normal (29γγ) in all cases excepting the hypochromic where it was naturally below the normal; in the majority of cases, it was between 35γγ and 40γγ.

The mean corpuscular haemoglobin concentration. This was over 30 per cent in the hyperchromic type and below 30 per cent in the hypochromic type.

Morphology of the cells. Most remarkable changes are seen in the blood smear. Megaloblasts, macrocytes, anisocytosis, poikilocytosis and vacuolated red cells were always present in plenty in all the cases. Nucleated red cells were very common. Among the megaloblasts, different variations were seen. The ordinary megaloblast, the still larger nucleated cell, the gigantoblast, megaloblasts with their nuclei undergoing fission, megaloblasts with the nuclei arranged as the spokes of a cart-wheel—all these varieties were met with especially in the severe cases. In a few cases Cabot's Rings were seen in plenty. The leucocytes also showed some variations. Myelocytes and pre-myelocytes were not uncommon in the smear while the polymorphs showed a rather larger number of lobes. Leucopenia is the rule.

The fragility. We determined the fragility in 64 cases. In all it was within normal limits.

Van Den Bergh reaction. The direct reaction was negative in all cases. The indirect reaction was positive in 72 cases. A quantitative estimation of blood bilirubin was not made. The urine showed traces of bile pigment in 12 cases.

Kahn and Wassermann reactions. In the 70 cases in which these were done negative results were obtained.

Gastric analyses. Unfortunately we were unable to make a

gastric analysis in all the cases. Only 20 patients were subjected to a fractional test meal. The results are as follows:

2 patients had normal hydrochloric acid.
2 patients showed complete achlorhydria.
16 patients had marked hypochlorhydria.

A fractional test meal after histamine injection was not made in the 2 achlorhydric cases.

Other findings. In this group of 103 cases there were no patients with enlarged liver and spleen suggestive of malaria or kala-azar. We were not able to obtain a history of chronic malaria or kala-azar from the patients either, so that these 103 cases are cases of macrocytic anaemia developing as a result of pregnancy and with no other complications except in 16 cases.

These 16 cases are of the macrocytic hypochromic group. All of the patients were found to be suffering from ankylostome infection as revealed by the examination of the stools. All of them were suffering from a very severe degree of anaemia with hypertension, severe degree of oedema and albuminuria, the blood-pressure varying from 160 to 200 mm. systolic. The urine in all cases was loaded with albumin. These cases stand out in marked contrast to the rest of the uncomplicated cases in which the blood-pressure was normal in most patients, below normal in a few, when the urine was free from albumin in the majority and only in traces in a few. In other words the cases with ankylostomiasis were also complicated by a superimposed pregnancy toxaemia.

Wickramasurya[13] has shown the predisposition of cases with ankylostomiasis to pregnancy toxaemia. We believe that these cases with macrocytic anaemia and pregnancy toxaemia have very grave prognosis. Unless efficient and immediate treatment is adopted the chances for the patient are indeed poor.

Dietetic Studies

The diets of these anaemic patients have been found to differ in no way from other normal patients admitted for confinement. Mainly, the deficiency is in the intake of fresh green vegetables and the poor quality and small intake of fat, suggestive of a deficiency of vitamins A, C and D. Among these 103 patients, there were 52 non-vegetarians and 48 vegetarians. Twenty-two out of the 52 non-vegetarians came from the richer classes. There is no lack of protein in their diet. We have not been able to find

TABLE IX.

No.	Haemoglobin (per cent)	Haemoglobin in grams	R.B.C. in millions	W.B.C.	Colour index	Volume index	M.C.V. normal 89 cμ	Urine albumin	Blood-pressure	
									Systolic m.m.	Diastolic m.m.
1.	12	2.0	1.2	4375	0.5	1.2	100.0	++	160	100
2.	25	4.0	1.45	5000	0.8	1.2	107.0	+	145	95
3.	<10	—	0.9	4375	—	1.1	111.1	+++	180	110
4.	<10	—	0.6	3125	—	1,5	114.3	+++	170	90
5.	20	3.2	1.3	6250	0.8	1.1	95.0	++	195	100
6.	10	1.6	1.09	5625	0.5	1.1	92.0	++	165	105
7.	24	3.8	2.25	5625	0.5	1.2	96.0	++	160	110
8.	10	1.6	1.0	5625	0.5	1.2	94.0	+	175	115
9.	10	1.6	1.1	5625	0.5	1.1	94.0	++	160	110
10.	10	1.6	0.6	5625	0.8	1.1	95.0	+++	180	110
11.	32	5.2	1.4	5000	1.1	1.2	110.0	+++	180	110
12.	10	1.6	1.0	6250	0.5	1.1	98.0	++	180	110
13.	16	2.6	1.2	4375	0.7	1.3	106.0	+++	190	120
14.	10	1.6	1.0	6250	0.5	1,3	115.0	+++	190	120
15.	10	1.6	0.8	3750	0.6	1.2	94.0	++	150	95
16.	10	1.6	1.3	3125	0.5	1.2	107.7	+	155	100

out any deficiency of vitamins B_1 and B_2. The disease is met with in all classes and communities. The diets in Bombay have been analysed by Wills and Talpade[14] and they observe that vitamins A and C are deficient.

Labour and Puerperium

Of these patients 80 out of 103 were confined in hospital. The rest went home after a course of treatment and we have not been able to follow them up. Premature labour is very common. Labour ensued in 62 per cent between the 32nd and 36th week. The remainder went on to term and were delivered. Excepting in 6 patients in whom the forceps had to be applied, the deliveries were all natural. The labour is usually quick and in no case was there any uterine inertia. In 2 patients the placenta was partially adherent and had to be removed. Twenty per cent of the patients developed mild degrees of puerperal infection showing how liable these women are to sepsis.

Maternal Mortality and Morbidity

These patients were under treatment in the wards for some time and so the results do not give the correct gross mortality for anaemia in pregnancy. Patients with severe anaemia are occasionally admitted into the hospital advanced in labour and such cases have not been included in this report. In the last 2 years the gross mortality from anaemia in pregnancy was 24.6 per cent. In this series, out of 80 patients, who were delivered in the hospital, we lost 6—mortality 7.5 per cent. Of the 6, one died during the course of labour, 3 died 12 hours after confinement and 2 died on the 3rd and 7th day respectively. In all these patients the haemoglobin index was between 10 and 25 per cent and the red blood cells 0.5 millions to 1.5 millions.

Twenty per cent of the patients developed uterine sepsis, 5 per cent developed urinary infection and 12 per cent had a mild degree of fever ranging from 99°F. to 101°F. for which a cause could not be found.

A few remarks may be made about the cases complicated with ankylostomiasis and toxaemia. In 4 of the patients, we had to induce premature labour. Six responded well to treatment—liver extract injection, and intravenous hypertonic glucose injections—the blood-pressure came down and the albuminuria cleared up in a week's time. The remaining 6 went into premature labour—the hypertension and albuminuria subsiding by

the 4th day of the puerperium. We were forced to induce premature labour in 4 patients in spite of the severe anaemia as the hypertension and albuminuria increased despite treatment. Artificial puncture of the membranes was the method adopted. All the signs cleared up by the 7th day of puerperium. We did not lose any one of these patients.

Foetal Mortality

Seventy children were born alive and 10 were stillborn, while 15 died during the neonatal period. Total mortality 31.3 per cent. It is remarkable that all the children born of these anaemic mothers had a normal red blood cell count and haemoglobin. We give below the average of 35 cases.

Table X.

	No. of cases	Haemoglobin (per cent)	R.B.C. millions
Babies of normal women (controls) ...	25	110	5·5
Babies of anaemic women	35	105	5·3

After confinement these patients are in a grave condition for the first few days and unless the patient is very carefully nursed, the heart may fail. Absolute rest in bed and continuation of treatment are essential. The rapidity with which these patients improve after confinement is really remarkable. We shall show at a later stage how patients who never responded to any form of treatment during pregnancy, improved rapidly with treatment after confinement.

The Follow-up

Of the 80 patients who were delivered in the hospital we were able to follow 30 up to 3 months. At the end of 3 months there was not one patient showing any of the signs of the macrocytic anaemia from which they suffered during pregnancy. An interesting feature of this is the fact that excepting for 10 patients, none took any medicine a month after their confinements.

Anaemia in Successive Pregnancies

Of the 103 patients 4 gave us a history of having had the same complaint in previous pregnancies. One patient had had 3 children, two 4 children and one 6 children.

One hundred patients suffering from eclampsia were treated during the same period. The average haemoglobin of these cases was 62.5 per cent and red blood corpuscles 3.2 millions. The blood smear was more or less normal showing occasionally a tendency to microcytosis. In 65 cases pre-eclamptic toxaemia was investigated from the haematological standpoint. The average haemoglobin was 63.6 per cent and red blood corpuscles 3.4 millions. The majority of patients in both groups had a haemoglobin over 60 per cent and red blood corpuscles over 3 millions. In no case did we encounter any severe grade of anaemia. On the other hand, not one patient of these macrocytic anaemias (excepting those complicated with ankylostomiasis) showed any sign of pregnancy toxaemia.

It has been suggested that anaemia is a cause of toxaemia. Our observations do not support this view.

TREATMENT

We do not propose to go into the details of the treatment but only to discuss some standard methods which are being employed the world over.

Macrocytic anaemia of pregnancy is essentially a deficiency disease. We believe that the deficiency is in the intrinsic factor and not in the extrinsic factor. This deficiency has to be made good and supplied to the mother by administering it in the form of liver or its various extracts. Early and effective treatment must be adopted and it must be the aim of every obstetrician to bring up the haemoglobin to at least 50 per cent and red blood cells 3 millions before the woman goes into labour. Otherwise the results may be disastrous. Wills[15] attributes this anaemia to the extrinsic factor deficiency and has reported excellent results with Marmite. We have tried Marmite in a series of cases and are unable to confirm her views. We shall discuss the treatment under the following heads:

1. Patients treated with Marmite.
2. Patients treated with impure liver extract.
3. Patients treated with pure liver extract.

PATIENTS TREATED WITH MARMITE

In 25 cases the patient was given one ounce of Marmite in 24 hours by mouth. In addition to Marmite, patients were also given 90 grains of ferri et ammonium citratis in 24 hours and

hydrochloric acid by mouth. Chart I shows the response to the treatment during 14 days. It is a chart typical for all the cases treated with Marmite. The average maximal reticulocyte response was 3.6 per cent, the average maximal haemoglobin increase was 5.6 per cent and red blood cells 0.25 millions after 14 days' treatment.

Wills[15] showed the importance and value of Marmite in pernicious anaemia of pregnancy and how a sharp reticulocyte response and marked improvement was noticed even in the majority of the severe cases. Napier also showed how Marmite gives very beneficial results in tropical macrocytic anaemia in men. Perhaps if the treatment had been carried over a much more prolonged period, beneficial results might have been obtained by us, but the majority of these patients are so very ill that such a delay would have proved disastrous. It is the duty of every obstetrician to see that such severe cases of anaemia are treated so effectively that the patient is in as fair a condition as possible to stand labour, which may come on at any time.

Patients Treated with Impure Liver Extract

The following liver extracts were tried:

1. Campolon (Bayer).
2. Neo-Hepatex (Evans).
3. Concentrated liver extract (Eli Lilly).
4. Garnick's liver extract.

In 85 patients one or other of the liver extracts was given. Our results have been very gratifying. All the drugs were given intramuscularly every day, the dosage varying from 2 to 5 c.c. according to the severity of the case.

Campolon. Chart II shows the progress of a case treated with Campolon. Fourteen patients were treated. The minimal number of injections given were 6 and the maximal 12. Marked rapid improvement occurred in all the cases except 2 of which special mention will be made later. The average maximal reticulocyte response was 26.8 per cent, the haemoglobin increase was 16.5 per cent and red blood cells 1.8 million after 10 days' treatment.

Neo-Hepatex and Eli Lilly liver extract. Twenty patients were each treated with Neo-Hepatex and Eli Lilly liver extract. Charts III and IV show the progress of a typical case in each group. Both extracts have given us good results. The average

maximal reticulocyte response to Neo-Hepatex was 24.2 per cent while for Eli Lilly liver extract it was 23.6 per cent. The average rise in the haemoglobin and red blood cells after 10 days' treatment was 12.5 per cent and 1.4 millions for Neo-Hepatex while for Eli Lilly liver extract it was 11.6 per cent and 1.2 millions.

Garnick's liver extract. We used this preparation on 15 patients. The progress of one case is shown in Chart V. With Garnick's liver extract, the results were not very good. The maximal reticulocyte response was 18.6 per cent, haemoglobin rise 8 per cent and red blood cells went up by 0.8 millions during the 10-days period.

The 25 patients treated with Marmite were given liver extract injections after the 14 days' treatment. Surprising improvement was the result. A typical chart showing the effect of liver extract in patients in whom Marmite failed is shown in Chart VI. We feel that one should not waste time in instituting efficient liver therapy in the treatment of the macrocyic anaemia of pregnancy.

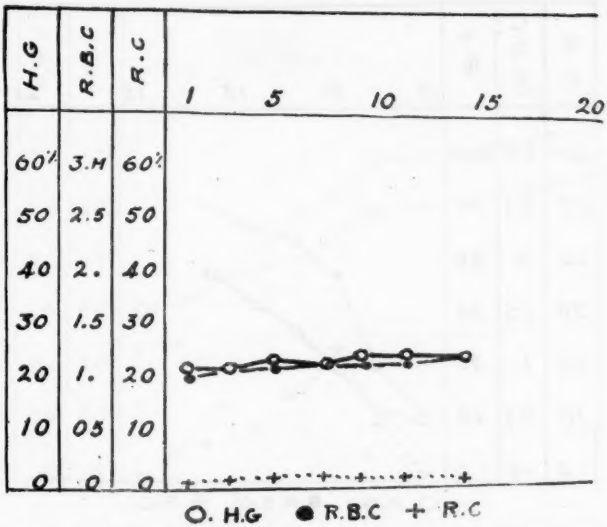
Treatment with pure liver extract. Treatment with pure liver extract in cases of tropical macrocytic anaemia has given rise to much discussion. We give below details of a few cases of severe macrocytic anaemia in pregnancy treated with pure liver extract. The number of patients treated are few owing to the cost of the drugs, but we find that the results we have obtained warrant their publication. We had very encouraging and excellent results with the pure liver extracts—better than with the cruder liver extracts.

The following preparations were tried: (1) Anahaemin (British Drug Houses), (2) P.A.F. Hepatex (Evans).

Anahaemin. Six patients with macrocytic anaemia were treated with Anahaemin. The method was to give 2 c.c. intramuscularly every 4 days for 4 injections—in severe cases the injections were given on alternate days. Not more than 5 injections were given in any case. Good reticulocyte response was obtained in all cases. The patients responded with greater rapidity than when cruder liver extracts were used. Chart VII shows a typical case treated with Anahaemin.

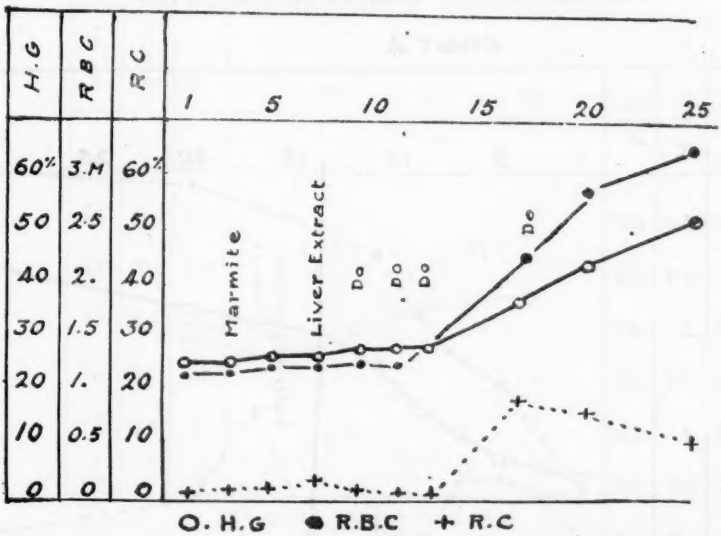
P.A.F. Hepatex. Six patients were treated with P.A.F. Hepatex. The method was to give 5 c.c. intramuscularly every 3rd day for 4 injections. Our results were very gratifying. In one case in which the cruder liver extracts failed to bring about any improvement in the patient's condition, P.A.F. Hepatex succeeded in bringing about a rapid improvement. Charts VIII

Chart. 1



A case of macrocytic anaemia. Treated for 14 days with Marmite. The reticulocyte response was poor and progress slow.

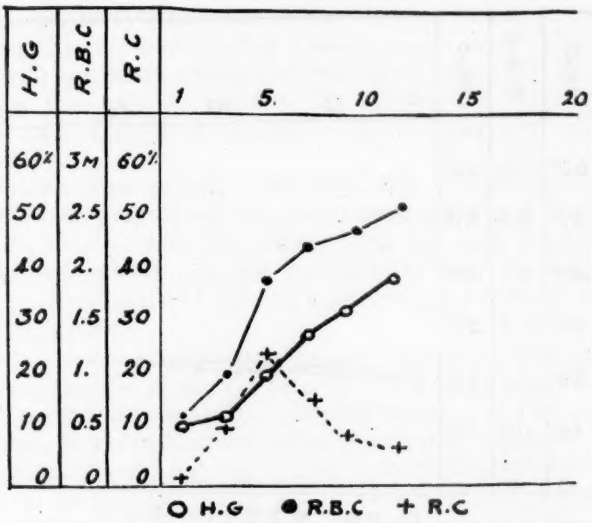
Chart. 2



A case of macrocytic anaemia. Chart showing the result of treatment with Campolon 5 c.c. daily.

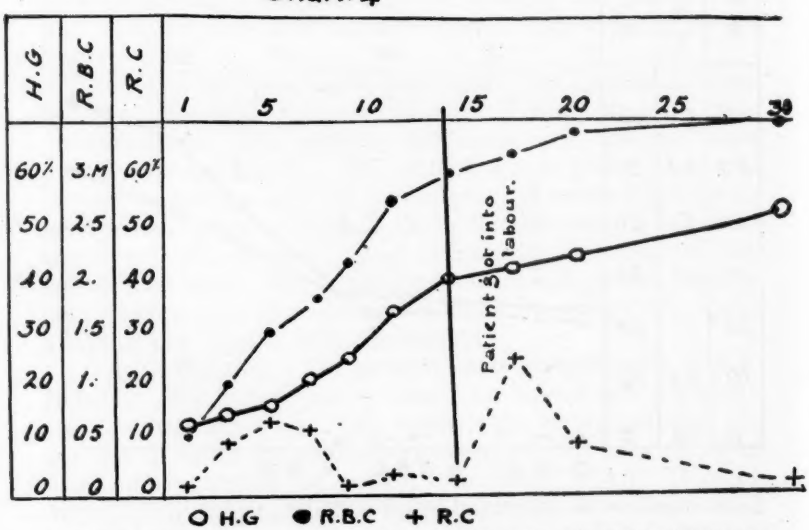
A.L.M.

Chart. 3



A case of macrocytic anaemia. Chart showing effect of treatment with 4 c.c. of Neo-Hepatex every day for 6 injections. Patient got into labour on the 14th day. Note the sudden rise in the reticulocytes immediately after labour. The blood smear at that stage showed all varieties of abnormal red cells.

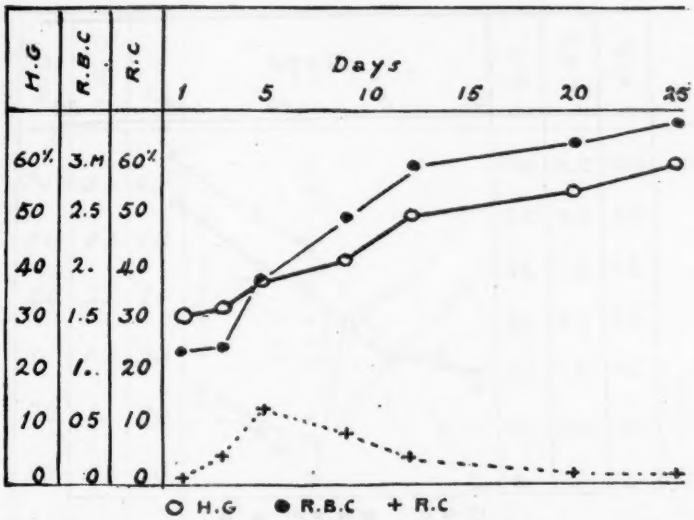
Chart. 4



A case of macrocytic anaemia treated with Eli Lily concentrated liver extract. She got into labour on the 12th day and delivered naturally a live child weighing 6 pounds. Puerperium normal. Went home on the 25th day.

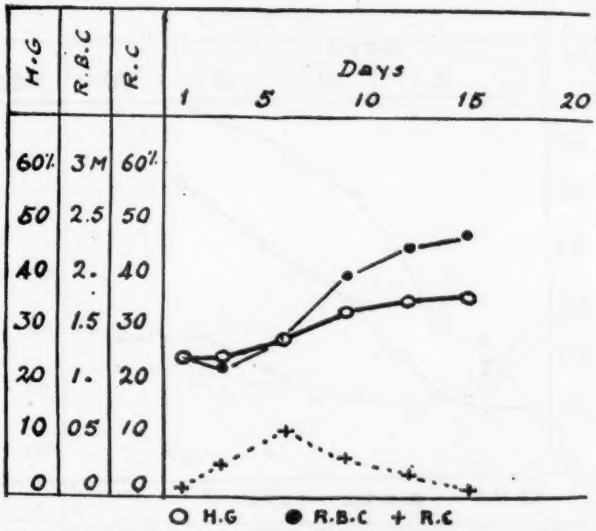
A.L.M.

Chart. 5



A case of macrocytic anaemia. Chart showing the result of treatment with Carnicks Liver Extract. The response is slower than with the other preparations.

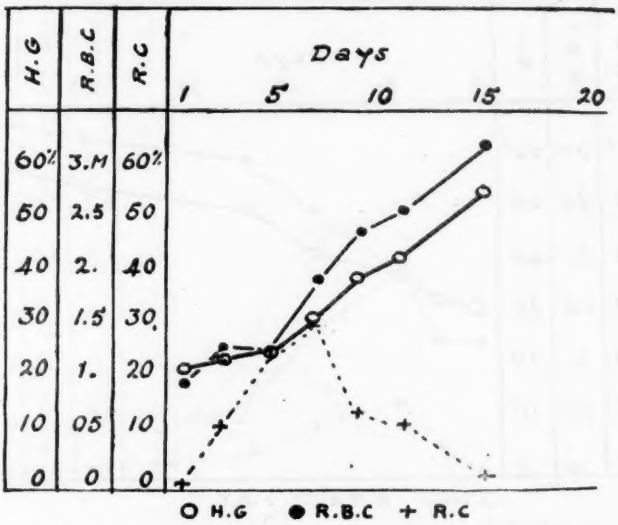
Chart. 6



A case of macrocytic anaemia. Patient failed to respond with Marmite treatment for 10 days, but rapidly improved with liver therapy later.

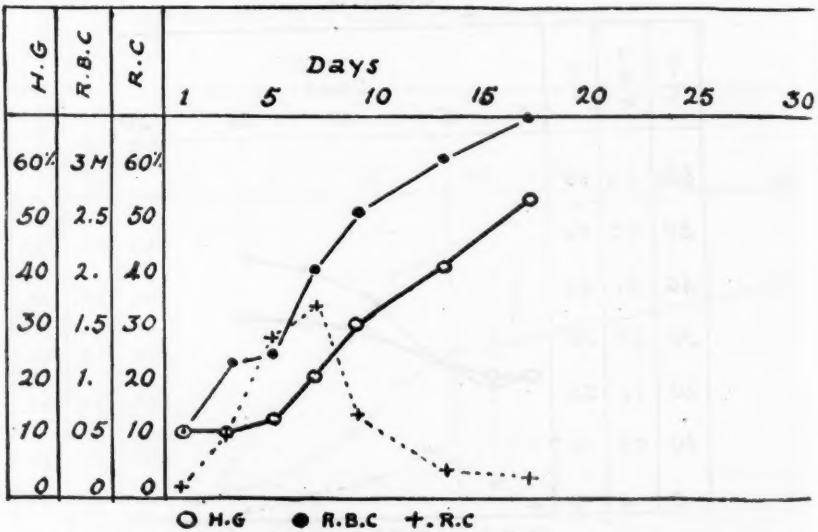
A.L.M.

Chart. 7



A case of macrocytic anaemia treated with Anahaemin.

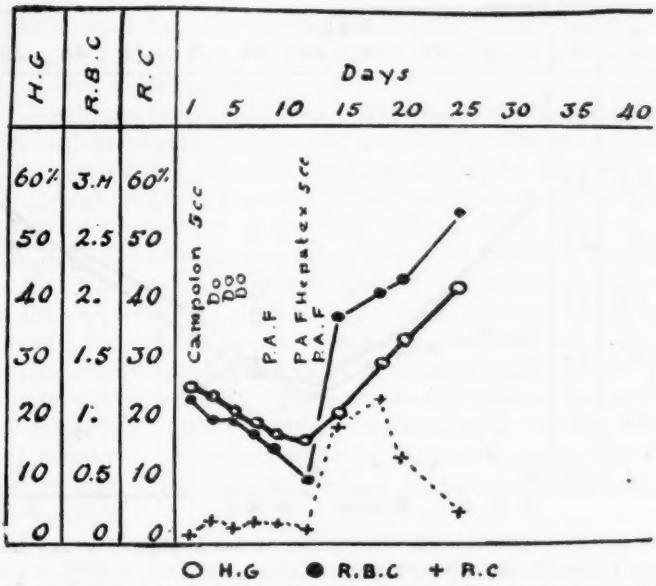
Chart. 8



A case of macrocytic anaemia treated with 5 c.c. of P.A.F. Hepatex intramuscularly every other day for 4 injections. Note the high reticulocyte response and the rapid improvement.

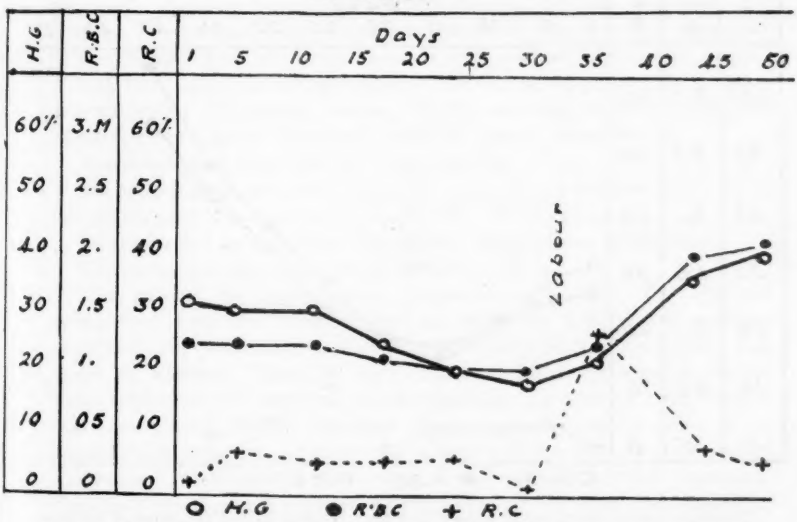
A.L.M.

Chart. 9



A case of macrocytic anaemia, where Campolon failed to improve the condition but patient improved with P.A.F. Hepatex.

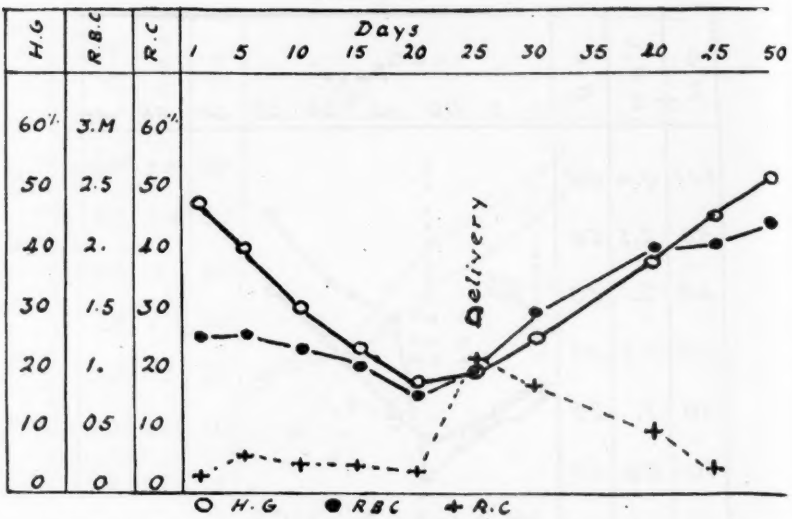
Chart. 10



A case of macrocytic anaemia where patient failed to respond to any treatment. Improved only after delivery.

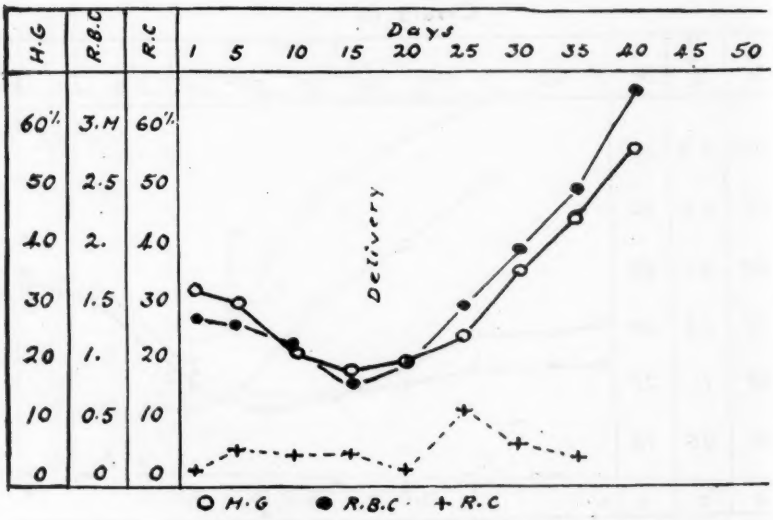
A.L.M.

Chart. 11



A case of macrocytic anaemia where patient failed to respond to any treatment. Improved only after delivery.

Chart. 12



Another case of macrocytic anaemia where patient failed to respond to any treatment. Improved only after delivery.

A.L.M.

and IX show the effect of treatment with P.A.F. Hepatex and the results with P.A.F. Hepatex in the case in which the crude liver extracts failed.

It will now be seen that our results are at variance with those obtained in tropical macrocytic anaemia in the non-pregnant. It is essential that intensive treatment should be adopted before the patient goes into labour and if we could bring up the haemoglobin index to about 50 per cent and red blood cells to 3 million, we feel much more confident about the future of the case.

As adjuvants iron and hydrochloric acid are useful especially in the hypochromic variety. In those patients with severe oedema, hypertonic glucose given intravenously helps to clear off the oedema much quicker. The dangers of labour and puerperium are well known. The collapse that follows the delivery, the dangers of sepsis and other complications do not require special mention. Treatment must be continued during the puerperium also. It is remarkable how rapidly they improve after confinement.

We now proceed to study some of the abnormal cases in the series. Below we give reports of three patients who did not respond to any treatment.

Case No. 1. Mrs. R., Muhammadan, aged 25 years; 4-para, 32 weeks pregnant. Previous pregnancies and deliveries all normal. Admitted into hospital on October 22nd, 1938, for oedema of the feet and weakness. General condition on admission, anaemic with puffiness of face and swelling of both feet; heart sounds rapid; haemic murmur heard all over; lungs clear; liver and spleen not palpable; uterus 32 weeks; not acting; foetal heart audible; blood-pressure 120/70; urine clear; albumin absent; faeces, no ova.

Haematological examination: vide Chart X.

Haemoglobin 32 per cent; red blood corpuscles 1.2 millions; white blood corpuscles 3125; colour index 1.3; mean cell volume 125 $c\mu$.

Blood smear: megaloblasts, macrocytes, anisocytosis, pokilocytosis.

Fractional test meal: no free hydrochloric acid.

The patient was given 4 c.c. Campolon every day. The maximal reticulocyte response obtained was 5.4 per cent, and as the patient's condition did not improve Fersolate pills and hydrochloric acid were given in addition. After 12 days' treatment blood examination showed haemoglobin 30 per cent; red blood corpuscles 1.2 millions. The patient was now given P.A.F. Hepatex intramuscularly. Even after 5 injections not only was improvement absent but the patient was seen to get worse. On November 15th, 1938, at the end of the P.A.F. injections, the blood examination revealed haemoglobin, 20 per cent; red blood corpuscles, 1.05 millions. She was now put on Ventriculin. On November 21st, 1938, haemoglobin was 18 per cent and red blood corpuscles 1 million.

A smear examination now revealed that the megaloblasts had disappeared. There were no nucleated cells at all. Since the patient was getting worse, we thought that the disappearance of the megaloblasts may be due to a state of aplasia of the bone-marrow. Unfortunately we could not do a marrow puncture. The question of a transfusion was now considered, but the patient suddenly went into labour and delivered a live baby weighing 6 pounds. Her condition was very critical for a few days but she recovered. Two days after confinement the blood smear revealed any number of megaloblasts and nucleated cells and from then on she improved rapidly with 2 c.c. injections of Campolon daily. After 5 injections on December 10th, 1938, her haemoglobin was 40 per cent, and red blood corpuscles 2.1 millions. She was discharged on December 21st, 1938, with a haemoglobin of 52 per cent, and red blood corpuscles 2.6 millions. Three months later her haemoglobin was 68 per cent; red blood corpuscles, 4.2 millions, and mean cell volume 84.6 cμ. She was not treated after she left the hospital.

Case No. 2. Mrs. D., Hindu, aged 28, 4-para, 30 weeks pregnant. Admitted for anaemia. Blood-pressure, 110/70; urine without albumin; faeces, no ova; liver and spleen not palpable. Blood examination: haemoglobin 48 per cent; red blood corpuscles, 1.3 millions; white blood corpuscles 4625; mean cell volume 123 cμ. Colour index 1.8 (vide Chart XI). Smear, megaloblasts + + +. Patient was given 2 c.c. Campolon every day along with iron and hydrochloric acid. After 15 days' treatment: haemoglobin, 24 per cent; red blood corpuscles, 1.15 millions. She was now given 5 c.c. Hepatex every day for 5 injections, at the end of which her haemoglobin was found to be 18 per cent; red blood corpuscles, 0.8 millions. The smear at this stage showed the absence of all megaloblasts and nucleated cells. A marrow puncture was not done. She went into labour the same day and delivered a stillborn child weighing 3 pounds. Her condition was very critical for 72 hours at the end of which a blood examination revealed the presence of innumerable nucleated red cells of all varieties. She was now given 2 c.c. Campolon injections every day and she improved rapidly. On the 10th day of the puerperium the haemoglobin was 26 per cent; red blood corpuscles, 1.2 millions. On the 25th day her haemoglobin was 46 per cent; red blood corpuscles 2.05 millions. On the 30th day at the time of discharge haemoglobin was 52 per cent; red blood count 2.8 millions. Three months later haemoglobin, 72 per cent; red blood corpuscles, 4.4 millions; mean cell volume 86 cμ. She did not take any medicines from a month after her confinement.

Case No. 3. Mrs. R., Indian Christian, aged 32, 3-para, 30 weeks pregnant. Admitted for anaemia, oedema and breathlessness. Blood-pressure, 110/70; urine clear; liver and spleen not palpable; faeces, no ova. Vide Chart XII.

Blood examination: haemoglobin, 32 per cent; red blood corpuscles, 1.4 millions; white blood corpuscles, 3125; mean cell volume 119 cμ. Colour index 1.1. Smear, megaloblasts + + +.

The patient was given 5 c.c. Campolon every day along with iron and hydrochloric acid. At the end of 10 days, haemoglobin 26 per cent; red blood count 1.2 millions. She was now given Anahaemin 2 c.c. every day for 4 injections. At the end of the injections haemoglobin was 18 per cent; red blood corpuscles 0.8 millions. Megaloblasts were not seen in the smear at this stage. She went into labour and delivered a stillborn foetus 3½ pounds in weight. The blood smear was full of nucleated cells 48 hours after confinement, and with Campolon injections from then on she rapidly improved. At the time of discharge, 25 days after confinement, her haemoglobin was 57 per cent and her red blood corpuscles 3.4 millions. Two months later, haemoglobin 72 per cent; red blood corpuscles 4.2 millions; mean cell volume 88.6 $c\mu$.

These three cases show that there are certain types of cases among the macrocytic anaemia of pregnancy which do not respond to the ordinary methods of treatment. The remarkable features of these cases are the continued fall in haemoglobin and red blood cells in spite of the intensive liver and iron therapy that was instituted, the disappearance of all nucleated red cells from the blood, the flooding of the blood with the nucleated red cells after confinement and the rapid improvement from then on with the ordinary methods of treatment. It is clear that pregnancy was the factor which kept any improvement in abeyance. The question that now arises is whether a transfusion would have helped. It might have, we did not do it and so we are unable to give an opinion. All the same it would appear that there are certain cases of macrocytic anaemia of pregnancy in which only termination of pregnancy would cause improvement in the mother's condition—just as in a case of pre-eclamptic toxaemia. Fortunately, these 3 patients went into premature labour and saved us from the dread of inducing labour in an anaemic woman.

We now give below the haematological records of a few patients who came in first with macrocytic hypochromic anaemia which later went on to the stage of macrocytic anaemia. Such cases are very rare indeed.

Table X shows in detail the results of the blood examination when these patients first came into hospital and a second time 6 to 8 weeks later. All the patients were treated with iron and hydrochloric acid. All of them remained in hospital for a week and went home improved of their own accord. Only 2 of the patients continued to take the medicines. All these patients were readmitted 6 to 8 weeks later suffering from oedema, dyspnoea and general debility. A blood examination at that time

TABLE X.

	1		2		3		4		5		6	
Case No.	1st Admission	2nd Admission	1st Admission	2nd Admission	1st Admission	2nd Admission	1st Admission	2nd Admission	1st Admission	2nd Admission	1st Admission	2nd Admission
Haemoglobin (per cent)	52	20	50	32	42	10	40	12	55	21	40	12
R.B.C. (mils.)	3.0	0.8	3	1.5	2.8	0.5	2.5	0.5	3.4	1.33	2.5	1
Colour index	0.8	1.2	0.8	1.1	0.7	1	0.8	1.2	0.5	0.8	0.8	0.6
Mean cell volume (cμ)	79	124	76	112	77.0	124.0	72	114	75.6	112	78.2	116
Smear	Microcytic anaemia	Megaloblasts +++	Microcytes +++	Megaloblasts ++	Microcytes +++	Megaloblasts ++	Microcytes ++	Megaloblasts ++	Microcytes +++	Megaloblasts ++	Microcytes +++	Megaloblasts ++
Period of pregnancy (weeks)	28	34	24	30	30	36	28	36	20	30	30	36

revealed macrocytic anaemia. All of them were treated with liver extract injections and improved considerably under treatment.

These cases show that a microcytic hypochromic anaemia in pregnancy if untreated or if not properly treated may go on to the stage of macrocytic hyperchromic anaemia. Two of the cases are of the macrocytic hypochromic variety. An inference that may be drawn is that a microcytic hypochromic anaemia passes through the stage of macrocytic hypochromic, before it becomes macrocytic hyperchromic anaemia. The 2 patients who continued to take iron and hydrochloric acid also developed the macrocytic anaemia. We may, therefore, suggest that iron by itself is not a sure treatment of the anaemia of pregnancy. It is true that the majority of microcytic hypochromic anaemias respond well to iron therapy; but it is well to remember that certain cases develop the macrocytic type in spite of iron. Such cases respond only to liver therapy.

We have not discussed the microcytic hypochromic anaemia of pregnancy in any detail in this paper. It is so very common in the antenatal patients here that as a routine we put all patients on iron.

Discussion on the Aetiology

A good deal of controversy exists concerning the aetiology of pernicious anaemia of pregnancy. The view is widely held that pernicious anaemia of pregnancy is a deficiency disease due to the deficiency of the extrinsic factor in the diet and since the report of Wills on the efficiency of Marmite in the treatment of these anaemias, this view has many adherents. We have shown, however, in our series, that none of the cases responded to Marmite but responded exceedingly well to liver extract injection both pure and impure. The haematology of these anaemias is exactly the same as the so-called tropical macrocytic anaemia as reported by Napier[16]; but with this difference, that while Napier's cases responded to Marmite ours did not; Wills observes that nutritional macrocytic anaemia responds less to pure liver extracts. Our patients though few responded very well to pure liver extracts—Anahaemin, and P.A.F. Hepatex. None of these pure liver extracts contain any of the extrinsic factor. And, therefore, we may suggest that the macrocytic anaemia of pregnancy is an intrinsic factor deficiency disease. Further, we have found this anaemia to be prevalent even among the middle and well-to-do classes among whom there is no question of an extrin-

sic factor deficiency. We may, therefore, be justified in suggesting that this anaemia of pregnancy is not an extrinsic factor deficiency disease especially as none of our cases improved on Marmite.

The anaemia is usually most evident in the last trimester when the foetal demands are on the increase. It is well known that the iron requirements of the foetus are taken from the mother as also the anti-anaemic principle necessary for blood regeneration. In the majority of pregnant women these demands are met with without any untoward effect on the mother. But in those in whom the supply is deficient, or who have a constitutional predisposition which prevents them from standing the strain of foetal demands like other pregnant women, these foetal demands produce various changes in the maternal organism. When the demand is for the iron alone and especially when the supply or the utilization or both are at fault, the mother develops the ordinary microcytic hypochromic anaemia so commonly found in pregnant women. At a later stage when the anti-anaemic factor has to be supplied and the maternal organism is unable to meet the needs of both herself and the foetus, macrocytic anaemia develops because, irrespective of the needs of the mother, the foetus acting as a parasite takes its necessary quota of the anti-anaemic principle from the mother. As a result of the foetal demands for the anti-anaemic factor there is an upset in the normal process of haemopoesis in the mother due to the relative deficiency of anti-anaemic factor available to the mother and this leads to the development of macrocytic hyperchromic anaemia. Occasionally, however, the demands for both iron and the anti-anaemic factor exist and in such cases the mother suffers from a relative deficiency of iron and anti-anaemic factor. Such a deficiency leads to macrocytic hypochromic anaemia which is not at all uncommon and which can be easily explained on the basis of the dual deficiency. We have shown how some of the patients never responded to treatment till delivery and how all recover their normal haemopoesis by the end of a few weeks after confinement. We are convinced that this variety of anaemia is essentially due to the pregnancy, to a relative deficiency of iron and to the anti-anaemic factor owing to the foetal demands. We suggest that the iron deficiency alone gives rise to the common microcytic hypochromic anaemia, the relative deficiency of the anti-anaemic factor gives rise to macrocytic hyperchromic anaemia and a dual deficiency of both iron and anti-anaemic factor to the macrocytic hypochromic anaemia.

We also suggest that the microcytic hypochromic anaemia is the earliest manifestation of an existing deficiency and this if not treated or improperly treated will lead to the macrocytic hyperchromic anaemia probably through the stage of macrocytic hypochromic anaemia. We have shown elsewhere how microcytic anaemia develops into the macrocytic type in spite of treatment with iron and how these patients later on respond to liver therapy.

It is surprising how the symptoms clear up under treatment with liver and how all patients are really cured soon after confinement. We are even tempted to think of anaemia of pregnancy as a variety of toxaemia of pregnancy because of the similarity in its progress and behaviour to the pre-eclamptic toxaemia. For

(1) Pernicious anaemia is essentially a disease of the 2nd and 3rd trimester of pregnancy.

(2) After confinement the disease clears up very quickly just as albuminuria and hypertension clear up after delivery in pre-eclampsia.

(3) Just as pre-eclampsia if untreated may go on to eclampsia, so also microcytic anaemia if untreated may go on to the macrocytic type.

(4) There are some cases of toxaemia in which induction of labour has to be resorted to since the patients do not respond to treatment. It would appear from a few cases we have had that only subsequent to the termination of pregnancy the mother's condition will improve with treatment.

We are at present advising all the pregnant women attending the clinic to take iron and some form of liver during the antenatal period. We hope to make a further investigation and see how far liver and iron combined will form a sufficient prophylaxis for this dreaded complication of pregnancy.

Pregnancy may occur in women who are anaemic due to various other causes—the usual causes of all anaemias—or a pregnant woman may become anaemic due to some other explicable cause as malaria, kala-azar, ankylostomiasis, bleeding haemorroids. But it must be borne in mind that pregnancy may aggravate the anaemia in these conditions. We believe that there is only one anaemia that can occur as a result of pregnancy —the anaemia of pregnancy—and we have given its characteristics above. We suggest a simple classification given below:

I. Anaemia incidental to pregnancy ("The anaemia of pregnancy")—

Microcytic—Hypochromic.

Macrocytic—Hypochromic, hyperchromic.

II. Anaemia, including all the anaemias met with in the non-pregnant.

Summary and Conclusion

1. An analysis of 103 cases of macrocytic anaemia of pregnancy is presented.

2. The anaemia is commoner in the multiparae than in the primigravidae.

3. It is essentially a disease of the 2nd and 3rd trimesters.

4. Macrocytic hyperchromic anaemia is more common than macrocytic hypochromic anaemia.

5. In the typical macrocytic anaemia of pregnancy there is not usually a severe albuminuria. But when ankylostomiasis complicates the condition, macrocytic hypochromic anaemia is very common and hypertension and albuminuria are very frequent.

6. Premature labour is very common and all efforts should be made to bring up the haemoglobin to at least 50 per cent before labour sets in. Labour in the very anaemic is fatal.

7. For this purpose efficient liver therapy must be instituted at the earliest possible opportunity. We have not found Marmite useful in this condition.

8. We have found parenteral administration of both pure and impure liver extracts effective. The dosage depends upon the condition. Iron and hydrochloric acid by mouth are useful adjuvants.

9. Still there are some cases of anaemia in which the patients do not respond to any treatment. Blood transfusion may be worth while trying in these cases. We have recorded 3 cases in which only the natural termination of pregnancy seemed to improve the condition.

10. We have shown how 6 patients with microcytic anaemia went on to the macrocytic type—2 in spite of treatment with iron. May we suggest that microcytic anaemia is the earliest manifestation of the severer type that may follow if neglected. We also suggest that though the majority of cases of microcytic anaemia respond to iron, iron by itself is no guarantee against the development of macrocytic anaemia. We believe iron in conjunction with liver extract is the best therapy for antenatal cases.

11. A follow-up of 30 patients has shown that at the end of 2 to 3 months all had an absolutely normal blood picture and the usual average haemoglobin percentage and red blood cells. Many of them did not have any treatment after leaving the hospital.

12. The anaemia behaves like pre-eclamptic toxaemia of pregnancy.

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Pruritus Vulvae: Leukoplakia and Kraurosis

BY

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I BEGIN by apologizing to readers of this journal for the limitations of my gynaecological experience. Although I have studied the skin diseases which affect the vulva for over 30 years, my chief work has been in private practice. That field provides a smaller number and less variety than is obtained in a large clinic, and gives little opportunity for the histological investigation which is so readily performed in a hospital. On the other hand, it has the advantage that one can carry out special lines of treatment with less interruption, and can watch the results over a more prolonged period of time, because the patients come for advice on other conditions.

In the space at my disposal, I shall discuss the skin diseases on and adjacent to the vulva which are frequently seen by the dermatologist, and contrast them with those which come more within the scope of the gynaecologist. Then I shall summarize briefly the varied views on the long-debated subject, leukoplakia and kraurosis, and explain how I formed certain conclusions after slow experiment with electrical methods used in the treatment of diseases of the skin and of women. Finally, I shall describe these methods and report a few typical cases.

PRURITUS VULVAE

As the causes of pruritus of the vulva are admirably set out in most of the modern gynaecological textbooks, I shall deal only with those which are accompanied by alterations of the epithelium which often develop into the conditions known as leukoplakia and kraurosis. For as long as I remember, even in my student days, I was interested in pruritus of the vulva, because of my sympathy with the sufferers whose malady revealed the hopelessness with which the majority of our profession then regarded the possibility of permanent cure, and the probability of malignant development. Fissures, cracks, and enormously swollen labia stand out in my memory. The patients came once or twice a week to have the region painted with weak solutions of silver nitrate; at home they used douches and anaesthetic

local salves. As the years passed, I recognized that many people were soothed, even cured, by simple applications such as oil and calamine lotion, or liniment. Others, on the contrary, had continual relapses, often just before or just after the menstrual period. Indeed, one distinguished dermatologist told me that these patients could be cured while they rested in bed, but that they relapsed as soon as they returned to ordinary life. Only after many years did I realize the importance of avoiding all scratching and local contamination.

I found little guidance in the literature on the subject. In gynaecological textbooks especially, the descriptions of the skin with leukoplakia were bewildering. When I visited gynaecological clinics in London, unfortunately I found but few patients with a condition which could shed any light on the problem. Thus I missed much which could have aided my gradual experiments with various forms of treatment. Especially do I regret that I was ignorant until a few years ago of the work of Comyns Berkeley and Victor Bonney[3, 4].

As far as electrotherapy is concerned I was most fortunate. My interest in electrotherapeutics began just before 1914, when the late Dr. Samuel Sloan taught me his methods of ionization of the cervix and uterus for the cure of discharge and haemorrhage. During the Great War, while working in France, I met many of the leading electrotherapeutists of Paris, and was much influenced by their enthusiasm for the results obtained by electrotherapeutic methods in diseases for which surgery had till that time been the sole alternative. After 1918, I was able to follow, at St. Bartholomew's Hospital, the progressive steps of the research on diathermy for pelvic disease which were carried out by the late Dr. Elkin Cumberbatch; his methods soon gained world-wide recognition. Diathermy enables one to deal with many acute and chronic inflammatory pelvic conditions in which ionization is impotent or dangerous. The D'Arsonval high frequency in vogue before 1919 was not so effective, and was much more difficult to apply than diathermy.

From experience with dermatology I recognized that many cases of pruritus were due to dermatitis, i.e. an inflammatory reaction to an external irritant, and that this was in most patients due to local contamination. A vaginal discharge containing staphylococcus aureus or trichomonas vaginalis leads to much irritation; so also may the passage of urine infected with *b.* coli. Glycosuria was a rare cause. The preponderance of causes due to an external irritant is explained by the fact that my

work dealt chiefly with patients who had been sent to me by practitioners and gynaecologists in order to give electricity a trial after the failure of curettage and other methods of treatment, and before a resort to surgery. Electrotherapeutic methods had provided me with a much-needed link in dermatological treatment.

Pruritus differs widely, not only in the appearance of the surface, but also with the cause. Sometimes little is seen except a mild degree of hyperaemia, even when the patient complains of severe irritation. In such cases it is important to remember the *rôle* played by the general health in the mental and emotional reaction to the symptom of itching. The power of resistance of the individual also varies with the balance of her nervous system and her psychological and philosophical outlook on life. The mental origin of disease has long been stressed by non-professional healing cults, and of recent years orthodox medicine also has tended to place, perhaps, undue emphasis on the influence of the mind in the aetiology of disease. Prolonged worry and states of tension obviously undermine the health as a whole and lead to exaggeration of the sensations of pain and itching. However, the opposite is equally true; anyone who suffers from pruritus for months or years is bound to become affected psychologically. If the physical cause can be eliminated, the psychological habit in a normally constituted individual is broken, and cure may be dramatically rapid. The general health plays quite as important a part when other than external irritants are in operation. For example, a vaginal discharge and contaminated urine are common, and may continue on and off for years without giving rise to pruritus. Then the advent of some malady which lowers the threshold of resistance, such as feverish illness or a septic focus, may provide the starting point from which severe pruritus begins. Thus it comes about that, in order to track down the internal cause of pruritus, we may have to search for a septic focus in the tonsils, teeth, gall-bladder, appendix or other organ.

A brief review of the skin conditions frequently seen by the dermatologist may prove useful. All may extend from the vulva to the adjacent skin.

Lichenification is very common. It is the change undergone by the skin when long subjected to scratching and rubbing. The area is dry, swollen, indurated; the surface resembles grain leather, the natural grooves being deepened and exaggerated, owing to the underlying swelling. The colour may be pink, dusky red, grey or white, depending upon the alteration of the

horny layer and the degree of congestion below it. Since lichenification is caused by prolonged scratching, it may develop from simple pruritus, or it may complicate an already existing disease, such as eczema. Eczema is liable on any part of the body to be subjected to much rubbing and, therefore, it often becomes "lichenified." This type of lichenified eczema is often associated with an irritating discharge. The labia may be enormously swollen, with oozing serum and crusts, and a white, sodden surface. The inflammation extends frequently to the adjacent skin. Patients have been sent to me with this lichenified eczema, mistakenly diagnosed as leukoplakia, with the prognosis of malignant disease in the near future; yet they have recovered with simple measures of protection, eradication of the causal discharge and local applications of ultra-violet light and the high frequency condenser electrode.

The uncomplicated form of lichenification is known as *neurodermatitis,* and it is very common on the nape of the neck. When the vulva is affected the patient rubs and tears at this region; the paroxysms of itching lead her to scratch when half awake. She may be unaware of this habit. The surface presents the same exaggeration of the natural grooves of the skin, sometimes a powdery scaling of the horny layer, and discrete, small shiny-topped papules are seen near the margin. There may be marked pigmentation. Under the name "lepidosis" Victor Bonney has a coloured plate depicting this condition[3]. The disease may exist for many years, but in spite of the friction to which the part is subjected, it is not a precancerous state. It may spread to the adjacent regions, even so far as the sacrum. In the folds it tends to become eczematized, and then shows the white surface which has led to the use of the term leukoplakia. The scratching, like nail-biting, forms a habit most difficult to arrest. The original pruritus may have been a form of mental tic, or it may have begun when there was a genuine disorder in the blood-stream, such as arises sometimes (as mentioned above) with a septic focus.

With *Intertrigo,* inflammation occurs in the natural folds of the skin, where, with warmth, moisture and friction, the opposed surfaces favour the growth of micro-organisms and fungi—the groins, perineum, armpits, intergluteal fold and under the breasts. Intertrigo may show only a vivid erythema, or a more severe reaction with the horny layer detached, leaving a raw surface with exudation and a fissure. Itching may be absent; if present, scratching occurs, with secondary eczematization or

lichenification. Intertrigo may be associated with streptococcal organisms or fungi infections. With the latter there may be marginal vesicles, with an undermined horny layer. The mycelium and spores are found on scraping this under surface and examining with a 1/6 lens after soaking in liquor potassae. The most common infection is the thrush fungus (óídium albicans). Its lesions spread rapidly over the whole vulva, groins, adjacent thighs and abdomen. The severity of the itching and the rapid extension aid the diagnosis.

Tinea cruris, due to the epidermophyton inguinale, also grows in the horny layer and causes marked itching. It begins as red maculopapules which join and form large patches with a scaly circinate margin. The margin is the most inflamed part. It spreads on the vulva, pubis, groins and perineum, and is also often found in other folds. On the thighs it may resemble tinea circinata. Between the toes, especially the 4th and 5th, the infected skin is sodden, white and easily detached. This infection (athlete's foot) is very common. The organism is supposed to gain entrance from the wet floors of bathrooms, or bath mats. Presumably infection of the groin is acquired from the towel which has been used to dry the toes; but it has also been found on unwashed lavatory seats.

Maceration of the horny layer occurs when a discharge soaks into any one of the above diseases. This white, sodden appearance is the probable explanation of the misleading description "leukoplakia is seen spreading to the thighs, groins and perineum" so often encountered in works on diseases of women.

Seborrhoeic dermatitis is due to invasion of the horny layer by the pityrosporon, the so-called "bottle bacillus" which causes dandruff on the scalp. In certain individuals the staphylococcus albus complicates matters, leading to an inflammatory reaction. Then are seen red or pink patches, round or oval in shape, with fading margins, fawny centres, greasy yellow scales, and an outlying region of follicular papules. Difficulty in diagnosis occurs only when the eruption is confined to the groins and scalp; usually it also affects the face and median line of the chest and back, parts with active sebaceous glands. Itching is absent except when there is secondary infection with streptococci; then eczematization sets in, with serous oozing and fissures in the folds.

Psoriasis is often hard to diagnose when it affects only the anogenital area, and when vulvitis is present. It has smooth, firm, dark, shiny and slightly raised patches with a clearly defined margin. On scraping the patch, typical silvery dry scales

are loosened. Lesions are usually present in other parts of the body.

Rarer diseases are: true leukoplakia, erythema multiforme, scleroderma, dermatitis herpetiformis, pemphigus, various types of ulcers, lichen sclerosus et atrophicus. With most of these diseases, lesions are present on other sites of the body and may at the same time affect the mucous membrane of the mouth. Elizabeth Hunt[9] has seen so many of the last-named that she contends that many cases of leukoplakic vulvitis are in reality lichen sclerosus; I have seen very few of such cases.

The condition most frequently seen by the gynaecologist is *vulvitis* or *vulvar dermatitis*. This may be due to an extension of inflammation from the vagina or ducts, or it may be a reaction to an external irritant such as a discharge from the cervix or urethra, contaminated urine, or less often to glycosuria, soaps, douches, dyes in the clothing. When the trouble originates from the urethra, the presence of a caruncle aids the diagnosis.

Before describing vulvar dermatitis, I should like to emphasize this fact: the dermatologist often sees its early stage, but very rarely the later stages. By the time the last stage has set in the patient would consult, not a dermatologist, but a specialist in diseases of women. Hence, I believe, the ignorance of the dermatologist about the prevalence of malignant disease in the final stage of leukoplakic vulvitis. The gynaecologist, on the other hand, having less experience of the milder forms of dermatitis, has indiscriminately labelled all conditions with a white surface leukoplakia; and he, therefore, tends to regard them all as precancerous. The misnomer has led to much confusion, not only in diagnosis but also in prognosis and treatment. Vulvectomy has been performed on many patients who could probably have been cured by the application of simple remedies.

The name *leukoplakia* ought to be reserved for true leukoplakia, which is common on the tongue, but rare on the vulva. Leukoplakia shows translucent, bluish white or grey streaks or patches, with edges sometimes abrupt, sometimes fading into the adjacent normal mucous membrane. Or it may show thickened, raised areas with a sinuous border; these may be detached at intervals and renewed. They may affect the vagina, even the cervix. Difficulty in diagnosis arises when there is associated vaginitis and vulvitis. In the absence of discharge the diagnosis is clear when raised white patches are seen on a vivid red base. Later, cracks and warty growths herald the onset of malignant disease.

Leukoplakic Vulvitis and Kraurosis

A great step forward was made when Comyns Berkeley and Victor Bonney[4] separated out the forms of vulvitis and suggested the name leukoplakic vulvitis. In a recent address Victor Bonney[3] gives a clear picture of the stages of leukoplakic vulvitis. This type of inflammation shows simultaneous changes in the epidermis and the underlying connective tissue. The area involved extends to both labia and the intervening sulcus, the posterior commissure, clitoris and hood; the inflammation may spread to the perineum and anus but never to the vestibule and vaginal wall, nor the skin of the mons. In the first stage the labia are red and swollen. In the second stage they are white, thickened, retracted, with hypertrophy of the epithelium, elongated interpapillary processes, lymphocytes, disappearance of the elastic fibres in the upper part of the dermis and an increase in the deeper part. In the third stage there is dense whiteness, with red cracks and flattening of the labia. Victor Bonney sums up thus:

> In the final stage the sclerosis of the connective tissue is complete. Very few cells are seen under the epidermis. . . . The area now presents a smooth shiny surface and the elevations of the labia and the hood of the clitoris have almost ceased to exist. Pruritus has ceased. In leukoplakic vulvitis permanent histological changes are occurring, not only in the epithelium, but also in the entire thickness of the connective tissue underneath it. Such coincident changes characterize all precarcinomatous states, amongst which leukoplakic vulvitis is one of the most impressive.

Kraurosis is a label concerning which there has been as great confusion as with leukoplakia. It has been employed to include many different conditions which have in common only one feature, that of contraction of the vaginal orifice. For many years I made this mistake and hence I cannot now distinguish from my old notes which form of contraction affected the patients. When at length I studied the literature on the subject I was able to piece together an illuminating array of the facts. For this reason I believe that it may be helpful to others to give a brief summary of the most important writings on the subject.

First and foremost I place the concise definition given by the great French dermatologist, Darier[6]:

> The term kraurosis should be reserved for progressive sclerosing atrophy of the mucocutaneous teguments of the vulva, leading gradually to stenosis of the vaginal orifice, and the disappearance of the labia minora, the hood and the clitoris, and the effacement of the labia majora. The mucosa of the

parts involved is smooth, shiny, dry; the colour is white, waxy yellow, red or spotted. Complication by leukoplakia is frequent; in such a case cancer is much to be feared. The principal pathological condition in kraurosis is suppression of the ovarian function by senile involution, by sclerosing atrophy or castration; syphilis plays a role in certain cases. One must not confuse kraurosis with simple vulvar leukoplakia, nor with the whitish coloration of the vulva from lichenification, which results from pruritus vulvae of long duration.

Breisky[5] was the first to draw attention to the condition of contracted vaginal orifice; not all of his cases were associated with deficient ovarian function. Darier commended the pioneer work carried out by Jayle, who wrote two long articles on leukoplakia[10] and kraurosis[11]. He limited the term kraurosis to an atrophic contraction which was due to several causes. He described a red and a white kraurosis; in some patients both red and white kraurosis existed together. This was an important contribution to our knowledge. In his paper are excellent coloured illustrations of both types of kraurosis, and of kraurosis combined with vulvitis and also with cancer. Red kraurosis is accompanied by a reddened urethra, or a caruncle, and with redness of the ducts near the urethra and the vaginal orifice. The histology of kraurosis varies according to the relative changes in the epidermis and the dermis. With leukoplakia the epidermis is chiefly involved; with kraurosis the dermis is affected, and this leads to progressive atrophy and sclerosis.

An excellent résumé of the work of French, English and American writers was published by Graves and Smith[8]. Their conclusion was:

> An extensive review of the literature indicates the difficulties arising from the conflicting terminology . . . the clinical and histological evidence here presented shows that kraurosis and leukoplakia used in the classic sense are phases of an identical process . . . the historical, clinical and histological evidence shows the intimate relationship to cancer.

They advise treatment of the cause, which they attributed to trouble in the genital tract, which lay often as high as the uterus. With this conclusion I am in agreement.

Taussig[15, 16] adopts the label leukoplakic vulvitis for a state with pruritus, pain on urination, with white areas and subsequent contraction and sclerosis. Kraurosis he defined as the later stage, when the leukoplakic vulvitis has led to obliteration of the labial and preputial folds; thus the condition was seen with deficient ovarian function, in old women or those whose ovaries had been

removed. He gives many excellent histological illustrations, showing a layer of thickened superficial cells, increased granular layer, acanthosis, elongated interpapillary processes, and much round cell infiltration in the connective tissue. Gradually there develops flattened papillae, decreased round cell infiltration, increased sclerosis and diminished elastic tissue. Taussig found that ovarian extracts, X-ray and radium were of no value. In about half of his cases warty growths appeared, becoming malignant; hence he advises vulvectomy.

Hamilton Montgomery,[13] writing from the dermatological point of view, advocates the limitation of the term kraurosis to the condition so clearly described by Darier. Montgomery published many figures illustrating the histological appearances of so-called leukoplakia, of kraurosis and also of pruritus vulvae with lichenification. The sections from which these studies were made were taken from patients on whom vulvectomy had been performed. He found that all three conditions can be distinguished, but that they often pass on, one into the other, both clinically and pathologically. He concludes: (i) Kraurosis is an atrophic process which may possibly lead to a malignant change; (ii) leukoplakia of the vulva is a hypertrophic process, definitely a precancerous dermatosis, which frequently results in a malignant state; (iii) pruritus vulvae with lichenification (neurodermatitis) is a benign form of inflammatory dermatosis which does not *per se* result in a malignant change. Treatment of pruritus vulvae with X-ray or radium gives temporary aid; if continued, it may lead to epithelioma of a high grade of malignancy. Montgomery also made a special study of lichen sclerosus et atrophicus, and found that it sometimes could not be distinguished from certain types of kraurosis histologically, but this fact did not imply that the same causes existed in both diseases. Lesions elsewhere on the body aided the diagnosis of lichen.

Fred Adair and M. Edwards Davis of Chicago[1] describe leukoplakia and kraurosis as stages of the same disease. Their coloured plates and figures show an early stage of hypertrophy and a later stage of shrinking. Their cases were few; only 0.24 per cent in a large gynaecological clinic. They occurred chiefly at the menopause or later. The condition, they believe, is due to several forms of infection, often connected with leucorrhoea, sometimes with parasites, fungi or yeasts. The urine and the urethra they do not refer to. However, to the dermatologist their illustrations show the "late contracted stage of leukoplakic vulvitis"; they do not illustrate the true kraurosis. As regards

treatment, Adair and Edwards Davis give a detailed list of results which are so unsatisfactory that their recommendation of vulvectomy can well be understood.

Lloyd Ketron and F. A. Ellis[12] summarize their own conclusions and those of previous writers. *Leukoplakic vulvitis* they define as a chronic inflammatory condition which passes through four stages: (i) pruritus, redness, swelling, excoriation; (ii) retraction, thickening, whiteness, decreased size of both labia; (iii) cracks, ulcers, tendency to malignancy; (iv) smooth, shiny, white vulvar surface; contraction of subepithelial tissues leading to disappearance of the labia minora and clitoris; cessation of pruritus. *Kraurosis* they define as an atrophic state with (i) white patches and a caruncle of the urethra; (ii) gradual appearance of a yellow colour of the mucocutaneous surface; (iii) much contraction of the vaginal orifice, thinning of the labia minora and obliteration of the clitoris; (iv) rarely pruritus, but the region is sensitive, especially to the passage of urine. Leukoplakic vulvitis, pruritus vulvae with lichenification, and kraurosis could be differentiated in the early stages, but all three might be present together. When the vulvar condition was due to scleroderma, the diagnosis could be made by the presence of sclerodermatous lesions on other parts of the body.

The observations of these two workers interest me, because they emphasized the fact that, owing to the marked degree of shrinking and contraction, the final stage of leukoplakic vulvitis resembles true kraurosis, and because they noted the association of a caruncle with kraurosis. They found that contraction might occur even in youth, and narrate the case of a child 8 years of age in whom the inflammation spread to the perianal region, all tissues from the clitoris to the fourchette being involved, both labia thickened, white and smooth. The illustrations accompanying this report depict the late contracted stage of leukoplakic vulvitis.

In civilized communities both leukoplakic vulvitis and true kraurosis are rarely seen, even in large hospital clinics. I had the opportunity of discussing these cases with Dr. Helen Hendrie, who had wide experience during her 19 years of work with native women on the Gold Coast. There leukoplakic vulvitis was very common. The patients were young married women who usually sought advice for dyspareunia. They had extensive inflammatory reaction in the vagina, with thickening of the vaginal entrance; the vulva showed white patches or extensive white areas with macerated white epithelial surface. These patients

rarely consulted Dr. Hendrie during the earlier stages of their malady, but there was always obtainable a history of pruritus, discharge and often of cystitis. The inflammatory condition, she said, was followed by a sub-epithelial infection, with subsequent fibrosis, which manifested itself within a few years with thickening of all the tissues, then shrinking or contraction. Even up the vagina, strong adhesive bands formed; the obstacle thus caused was often so great that there was difficulty in passing a douche nozzle through the narrowed orifice. Thus, without having any knowledge of the literature on the subject, Dr. Hendrie described to me the stages of leukoplakic vulvitis. Native women were very susceptible to infection, Dr. Hendrie considered, on account of the low vitamin content of their diet; this consisted chiefly of inferior maize, koko yam and kassam. Whether malignancy might have developed later in life remained uncertain; most of these women die at a comparatively early age.

It would clarify matters if the term kraurosis were restricted to the condition defined by Comyns Berkeley and Victor Bonney and by Darier: contraction of the vaginal orifice, hardening, glistening or shiny whiteness, atrophy and gradual obliteration of labia minora, clitoris and hood, extending to the vestibule and to the fourchette. There is associated redness of the urethra, often a caruncle and telangiectatic patches on the mucous membrane. In some cases yellow plaques develop; they appear as if formed just below or within the mucous membrane. These yellow areas may come, then vanish, and others may be seen a few months later. I have not come across any references in the literature to the temporary nature of these yellow patches; had I not had the opportunity of watching the same patient over a period of many years I should not have discovered this fact. I published full details of this case in the *British Journal of Dermatology*;[14] since that report a yellow patch has begun to form again (July 1941), not connected with the small fissure for which she sought advice.

Does kraurosis have any symptoms in itself? I believe not. Several observers mention the fact that pruritus disappears, but that there is sensitiveness to the passage of urine. I believe that any symptoms are due to a superimposed infection which occurs from time to time. There is a normal degree of atrophy in old age; the mucous membrane is thinner, and looks pale and shining, having fewer epithelial layers. It is reasonable to suppose that the region is, therefore, more vulnerable to trauma and infection. If the urethra or the urine is infected, or there is

any discharge, the patient complains of sensitiveness and/or pruritus. Scratching and rubbing cause abrasions, fissures and ulcers. These permit the entrance of sub-epithelial infection, with consequent sclerosis and contraction. The condition resembles senile vaginitis, with its glistening mucous membrane and red patches, some of which are due to the blood vessels showing through the thin areas. Later, with infection, filmy adhesions form, which may develop into firm hard bands extending across the vagina. If kraurosis were, as many contend, due chiefly to deficient ovarian function, it would be common. On the contrary, it is very rare. The atrophic condition of old age does not cause any symptoms. The patient consults a doctor only when there is discomfort; in my experience this arises often from the flare-up of infection from an intra-urethral duct, or from the *b.* coli cystitis which is so common. Doubtless other causes also operate, such as cervical discharge. Long intervals may elapse between periods of re-infection. I have observed this especially when the caruncle is small and comparatively pale; when it is large and angry, the infective bouts may be expected to be more frequent. The patient may seek advice on account of sensitiveness to the passage of urine.

In brief, kraurosis is vulvitis occurring in elderly women and in younger women from whom the ovaries have been removed; in both cases pre-existing atrophy prevents the development of the hypertrophic stage with the keratinization seen with leukoplakic vulvitis. Oestrin preparations aid by rendering the part more vascular, and hence softening the sclerosis and diminishing the contraction. Too often, as the records show, the relief is only temporary. The relapse of symptoms occurs when local foci of infection become active.

Treatment of the Early Stage

When the foci of infection are suspected, examine the urethra and the genital canal. The urethra may require treatment, even when to casual inspection all seems healthy. Pressure on the anterior vaginal wall may express a cloudy fluid, or on passing a probe tenderness is elicited. If there is an active caruncle, redness or pouting of the urethra, infection of some intra-urethral duct is usually present. Benefit is rapidly obtained by ionization of the urethra. For this a preliminary local anaesthetic is given; I use Novotux. Wool is wrapped tightly round a fine copper wire to 1½ inches from the tip. The wire is attached to the positive pole of a galvanic battery, and introduced 1½ inches

PRURITUS VULVAE: LEUKOPLAKIA AND KRAUROSIS

(if possible) into the urethra. Two, four or six m.a. are passed for 2 to 5 minutes, once a week, for 2 to 4 doses. This is usually sufficient. In cases with a large granuloma, or with polypi, diathermy fulguration may be required. Vaginitis and cervicitis must be dealt with thoroughly; so must all angry ducts near the vaginal entrance. Thus only can one prevent the recurrence which can extend even from the smallest source of infection. Piles and perianal dermatitis demand special treatment; the methods of approach available cannot be described here.

Treatment of the Late Contracted Stage of Vulvitis and of True Kraurosis

Locally, only soothing applications such as a lotion of liniment of calamine should be used. Various anaesthetic remedies give temporary relief to pruritus. Fissures are painted with weak silver nitrate once or twice a week. As in the treatment of the early stage, the infecting source must be tracked down and dealt with as described above.

To soften the contracted tissues, I advocate pelvic diathermy. I employ the method introduced by the late Dr. Elkin Cumberbatch. What is its action? In all parts of Europe and America it has been acknowledged as an effective means of treatment of menopausal arthritis. During a course of such diathermy there is often a resumption of the arrested menstrual cycle; this would imply that it stimulates the ovarian function. Pelvic diathermy has yet another effect, which may account for the manner in which it softens contracted tissues; large, chronic inflammatory masses which fill the pelvis often disappear after a month or six weeks' treatment. So also, after a few doses, does the hard band round the vaginal entrance undergo resolution. I use small doses: 0.7 to 1 ampere for 15 or 20 minutes, given daily for a week, then twice a week for 3 or 4 weeks. The change begins before it seems possible that the improved ovarian function could have been the chief factor in operation. On the Gold Coast, Dr. Hendrie had no diathermy and tried various methods to induce pelvic congestion. She gave glycerine drainage, and ordered the patients to squat for an hour every evening in a shallow bath containing water as hot as could be borne; a kettle of boiling water replenished the bath and maintained the high temperature. When the contraction was severe, this treatment had to be continued for some months; it was almost always successful.

The beneficial effect of diathermy is brought about rapidly, and is very enduring in true kraurosis. In leukoplakic vulvitis

relapses are not uncommon, because the sources of infection tend to recur and patients do not always seek advice at the earliest symptom.

Method. A leaden belt is folded round the pelvis at a level mid-way between the anterior superior spine and the great trochanter; an all-metal electrode, attached to the other pole, is placed up the vagina. Sometimes, instead of the belt, I use a large leaden plate over the abdomen. The all-metal electrodes are of several sizes. In the case quoted below, the contraction was so great that at the first dose only the smallest electrode could be used; this had the diameter of a lead pencil. By the 7th dose, at the end of a fortnight, the largest electrode (diameter 1½ inches) was easily introduced. This patient remained well when I last heard from her 8 years later.

Oestrin Medication

Oestrin is much in favour as it brings about tissue softening in true kraurosis. It often causes local hyperaemia and discomfort for a few days at first. One of my patients, *aet.* 78, took in error four capsules of 3000 units of Menformon within 24 hours; she had a profuse mucous discharge, much local discomfort, and felt very ill for several days. A study of the literature reveals that although senile vaginitis and the contraction of senile kraurosis benefit from oestrin medication, it appears that the patients often return with recurring discomfort and pruritus. Although oestrin aids the combat with local infection (as for example in senile vaginitis and the gonococcal vaginitis of children) quite a number of cases of pruritus obtain little or no benefit, even after many months of its administration. Writers advocating the use of oestrin for leukoplakic vulvitis and kraurosis often admit that patients are "relieved," not "cured." Is this explained by the fact that the source of infection has not been removed, and that this often lies in the urethra?* As a rule treatment is not directed to the urethra in women, except when there is gonococcal infection. Another frequently unsuspected source of infection comes

*Since writing this paper I have seen the article by Winsbury-White on frequent micturition and enuresis in children. The girls usually had evidence of chronic inflammation of the urethra, vulvitis and inflammation of the mouths of the glands opening near the labia minora. As a rule the urine was free from infection. These findings agree in every detail with those which I have observed in young adolescent girls, and in women of all ages who have a long history of frequency of micturition. (Winsbury-White, H. P., *The Lancet*, 1941, ii, 331).

from the Bartholin and the para-urethral ducts. From any such focus, trouble may flare up when resistance is lowered. Streptococcal vulvitis often relapses without apparent local cause, just as streptococcal dermatitis does in other parts of the body; in the near future sulphonilamide therapy should prove valuable in this condition.

Objections to the employment of oestrin have been made. Little is known regarding the ultimate result of prolonged oestrin administration; the incidence of cancer demands careful consideration. Gemmell and Jeffcoate[7] state:

> There is evidence that ovarian and possibly pituitary hormones are concerned in the aetiology and development of malignant tumours in the breast and the uterus.

During the three years before 1940, these authors treated 43 cases of senile vaginitis and kraurosis vulvae with oestrogenic hormone. Three of these patients developed cancer of the cervix; 2 were aged 45, 1 was 53. They advise that oestrogenic therapy should be administered with caution if the cervix is infected or lacerated, and not at all when there is a family history of cancer. Nor do they approve of the use of oestrin in "leukoplakia vulvae," which they regard as a precancerous state. They quote authors who found that the metaplasia in the cervix which results from oestrogenic treatment may be prevented by the simultaneous administration of progesterone. Others advising caution are Auchinloss and Haagensen[2], who report in detail a case of cancer of the breast possibly induced by oestrogenic substances. Meanwhile, thousands of women are treated with oestrin for months or years; apart from the expense, is this necessary? Is it advisable? I published a case[16] of eczema vulvae in a woman of 49 who grew steadily worse with 35 strong progynon injections given twice a week; she was cured in 6 weeks with ionization of the cervix. The slight mucous discharge which caused her pruritus had been regarded as innocuous.

Man's interference with nature is often followed by unforeseen retribution. Therefore, I advocate a trial of pelvic diathermy which (in my admittedly few cases) has proved so efficacious in restoring contracted tissues, whether due solely to inflammatory fibrosis (leukoplakic vulvitis), or contributed to by deficient ovarian function (true kraurosis). Another advantage of diathermy is that its softening effect in true kraurosis appears to be so enduring. However, it must be remembered

that as diathermy cannot cure any form of infection except that of the gonococcus, all other organisms have to be otherwise dealt with.

Below are quoted brief reports of two typical cases of true kraurosis:

Mrs. B., age 66, came with a diagnosis of leukoplakia in February 1933. She gave a history of pruritus, and of discharge from time to time, for over 15 months. One ovary had been removed at the age of 30, but menstruation had been normal and the menopause had set in late. The labia majora were swollen, due to scratching, but did not show any white patches. Vestibule and labia minora shrunken, hard, glistening white; fissures posteriorly and to the left; telangiectatic patches near the urethra. Vaginal entrance so contracted that only a pencil-sized electrode could, with difficulty, be introduced. Paroleine and almond oil dressing ordered. Diathermy was administered on February 1st, 2nd, 3rd, 6th, 8th, 17th and 23rd. By the fifth dose pruritus had gone; by the seventh dose the fissures were healed, all looked softer, and the largest electrode was easily inserted (diameter 1¼ inches). In March four doses were given. In all, she had 11 applications, and appeared almost cured. On July 4th she came for neuritis, and had a few purpuric patches on the labia minora. Otherwise the vulva looked healthy, no longer white or hard. Seen next in January 1934, six months later; vulva showed the normal pale pink of age, no hardness or contraction; but she had two fresh purpuric patches, one with a bulla. In July 1939 she called at my request to show how the vulva had remained without any further treatment during the five years. All seemed normal for her age—no shrinking, hardness or pallor. She told me that when she first came to me she had no idea that there was contraction, but had seen with a mirror that the area was extremely white. I wrote to her in July 1941 and she replied from the country that thanks to my diathermy she had had no return of irritation nor of the unhealthy whiteness or hardness. She had had no further treatment of any sort; she is now aged 72.

Mrs. G., age 68, was sent to me in 1933 with marked kaurosis. The vaginal entrance was so hard that the examining finger appeared to be gripped as if with a tight ring; the firm band extended up for an inch. The urethra was involved also, hard and white. There was a history of cystitis a few months previously, with haematuria. Piles and perianal dermatitis were present, with an intergluteal fissure and sodden epithelium. After eight doses of diathermy all looked softer and more normal. She wrote to me six years later that there had been no recurrence of skin trouble, but the recent Munich crisis had caused some return of irritation. She went to Scotland, and I have not been able to trace her.

For a patient who left London at the beginning of the war, I advised a trial of oestrin. Her doctor reported that oestrin made the pruritus much worse, but there had been much improvement

of the atrophy and hardness during its use. He had tried several favourite preparations and been most disappointed with their effect on the pruritus. No doubt there had been in that case a recurring infective focus which had not been treated.

In the *British Journal of Dermatology* I reported the details of the case of an old lady whom I observed over a period of 8 years. Here is a summary of the points of interest in her progressive stages of vulvitis:

Mrs. B., age 72, sent for "leukoplakia," was really in the early stage of contraction of "leukoplakic vulvitis." At first I labelled her condition as kraurosis, because there were hard white parts with great contraction of the vaginal orifice. There was also evidence of former urethral trouble, but this never again lighted up, and the caruncle remained small and pale pink. A few telangiectatic patches developed, later becoming deeply pigmented. From time to time she came with attacks of discomfort, tenderness on passing urine, usually due to fissures in the hard white sclerosed tissue at the orifice of the vagina. From these fissures faecal streptococci were found on several occasions; they always disappeared with soothing applications and diathermy. At first the orifice was too small to allow the passage of any instrument larger than a pencil; but very soon she took the largest electrode. She suffered from bronchial catarrh and "influenza" and spent much time in bed during the winter months. While her health was thus below par she tended to have more recurrences of the fissures than during the summer. At one time she developed two large yellow patches, which are said to be typical of true kraurosis. These completely disappeared during the first winter of the war, which she had spent in the country and had remained in better health than when in town. In July, 1941, she had a fresh small yellow patch, but otherwise the region is more normal than when first seen, but is still white, atrophied and sclerosed in part. She is now 80. Treatment consisted of a first prolonged course of diathermy, then gradually shorter courses as the years passed and the recurrences of the fissures became fewer. Latterly, she came for a short course twice a year. The doses were always small: 0.7 ampere for 15 or 20 minutes. After the first course there was never any difficulty in introducing the largest electrode. No oestrin was given except for 5 weeks whilst she was in bed with phlebitis during the winter before the war.

This case provides a marked contrast to the other two. Here the recurring infection led to fresh fissures; often the dermatitis extended to the groins, perianal and intergluteal region. At times the sclerosis threatened to become severe; the result of diathermy in softening the tissues and in healing the fissures was most impressive. But diathermy cannot cure recurring streptococcal dermatitis. Observation of this patient over 8 years

taught me much about the connexion between the contracted stage of vulvitis and of kraurosis.

No further work can be carried out with diathermy during this war; its waves interfere with the signals of the Royal Air Force upon which the future of our Empire and civilization depend.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

D.R.C.O.G., March 1942.

THE following candidates satisfied the examiners for the Diploma of the College:

Jean Rosemary Campbell Burton-Brown, London.

Mona Mary Davin-Power, Sunderland.

Margaret Mabel Flecker, Cumberland.

Perla Greeves, London.

Stephen John Hadfield, R.A.F.

Dorothy Myrtle Hicks, Leeds.

Christia Felice Lucas, Walsall.

John Kenneth Martin, Gloucester.

Florence May McClelland, Belfast.

Robert James Mitchell, Farnworth, Lancs.

Eileen Elizabeth Perry, Belfast.

Eric Eli Rawlings, R.A.M.C.

Joyce Mary Scholefield, Burnley, Lancs.

Edith Scott, Plymouth.

Horace Arthur Shaw, R.A.M.C.

Dorothy Margaret Shotton, Bristol.

REPORTS ON HOSPITALS AND DEPARTMENTS OF PUBLIC HEALTH

ROYAL SAMARITAN HOSPITAL FOR WOMEN, GLASGOW. MEDICAL REPORT, 1940.

THIS report is very well tabulated and it is obvious that a great deal of work must have gone into its compilation. Table V, Pathological Conditions, includes not only the disease, number of cases and deaths, but also average age, number married, details of parity under four headings, number of cases in which operation was performed, average number of days in hospital, number of cases in which the disease was primary, number of cases in which an additional lesion was present, and number of cases in which two additional lesions were present.

It seems a pity that a table giving details of the operations was not included, as this would have been of much greater interest than some of the factors mentioned above. The mortality table is well drawn up, and completed with a summary.

During the year 2,296 cases were admitted, and 2,118 operations were performed with a mortality rate of 1.18 per cent. Reports are included from the pathological, radiological, and deep therapy departments.

ROTUNDA HOSPITAL REPORT, NOVEMBER 1ST, 1939, TO OCTOBER 31ST, 1940.

As we had expected, this is an excellent report. It commences with a brief *résumé* in which the main points of interest in each particular class of case are given, followed by the details in table form. It is of particular interest, being the last report during the mastership of Dr. Davidson, and in many instances he has collected his seven-year results.

The new nurses' home, out-patient department and students' quarters, together with new equipment for the hospital, were all paid for by £160,000 made available from the Irish Hospital Sweepstakes.

During the year 3,293 patients were delivered in the hospital, and 1,574 in the district with 18 deaths. The mortality rate was 0.5 per cent and the morbidity rate was 3.67 per cent calculated on the British Medical Association standard.

The following points have been selected from among a flood of information. Out of 210 inductions of labour, 53 were for disproportion. Trial labour does not seem to find favour, but the results of induction must be very satisfactory since the incidence of Caesarean section for disproportion was only 0.7 per cent during the past 7 years. In the 7 cases of accidental haemorrhage, Caesarean section was performed with two deaths. This tends to support the view that surgery has little place in the treatment of this condition.

One Caesarean Wertheim's hysterectomy was performed with a satisfactory result. It is interesting to see that pubiotomy was performed on two occasions for disproportion.

The gynaecology section would be better if it included a table of diseases. The proportion of total to sub-total hysterectomies is impressive at 29 to 1 but there seems to be a preference for a perineal approach since vaginal hysterectomy was performed on 35 occasions.

With 623 admissions, the incidence of cervical carcinoma seems to be remarkably low at 5 cases, but this is probably accounted for by the apparent absence of radium in the department.

The report concludes with brief accounts of the work done in the paediatric, pathological and radiological departments.

NATIONAL MATERNITY HOSPITAL, DUBLIN. CLINICAL REPORT, 1940.

THE report is well arranged, the classification being straightforward and simple to follow. There were 2,896 patients delivered in the hospital during the year with a maternal mortality of 0.5 per cent, the morbidity rate being 2.35 per cent, British Medical Association standard.

The treatment of eclampsia with magnesium sulphate continues to give satisfactory results in the authors' hands, twenty-one cases being treated during the year with only one death.

Extensive use is being made of the lower segment Caesarean operation, out of 38 sections only 4 were of the classical variety. Two cases of placenta accreta are recorded, in both cases the uterus was perforated while manual removal was being attempted and in both hysterectomy was performed with satisfactory results.

An unusual case of a ruptured Meckel's diverticulum is described; it gave rise to a fatal peritonitis during the puerperium.

It seems a pity that, with 679 cases, the gynaecological report is still compressed into two pages and that a table of diseases is not included. Six hundred and one operations were performed with 3 deaths, giving an operative mortality of 0.5 per cent. Of the abdominal operations there were 81 Gilliam's ventral suspensions, sixty-one hysterectomies (including Wertheim's operation) and 31 myomectomies. The report concludes with brief details of the pathological work done during the year.

THE WOMEN'S HOSPITAL, SYDNEY. MEDICAL AND CLINICAL REPORT. JULY 1ST, 1939, TO JUNE 31ST, 1940.

THIS is a well-balanced report, and we are delighted to see that the gynaecological department has a fair share of the available space. The maternal mortality rates for the year were 0.177 per cent for booked and 9.30 per cent for emergency cases. In the last 8 years there have been only 43 deaths among 20,375 booked cases. Mortality rate of 0.211 per cent, a most satisfactory figure.

During the year there were 21 cases of eclampsia with 2 deaths; in both cases the onset of symptoms was antepartum. Manual removal of the placenta was performed on 66 occasions, which seems to be rather a high figure. But none of the cases figures in the mortality table.

The paediatric report is excellently set out with complete tables of stillbirths and neo-natal deaths. The mortality rate among the premature babies was 19 per cent.

Seven hundred and sixty-six patients were treated in the isolation wards, with 10 deaths. Only a small number of cases had puerperal sepsis, the majority being composed of incomplete abortions.

The gynaecological department dealt with 451 patients and 394 operations were performed with 4 deaths giving an operative mortality rate of 0.99 per cent.

As a wartime economy, many of the tables have been replaced by summaries of results but the complete tables have been drawn up and are available to anyone requiring them.

THE COOMBE LYING-IN HOSPITAL. CLINICAL REPORT, 1940.

A WELL-PLANNED report commencing with a short introduction, followed by Table I, which gives an outline of all the cases, the details being set out in the following tables. We were somewhat disappointed to find that the gynaecological department was given only the last of 48 pages.

During the year 1,546 patients were delivered in the hospital with a mortality rate of 1.03 per cent, and a morbidity rate of 3.3 per cent. Eleven cases of eclampsia were treated without a death. Of the cases of acute pyelitis, one was complicated by a congenital hydronephrosis and was treated by ureteral drainage.

There were 491 admissions to the gynaecological department and 398 operations were performed with only 2 deaths, giving an operative mortality of 0.5 per cent. We notice that the Alexander Adams operation is being used just as frequently as Gilliam's method.

Only 4 cases of cervical carcinoma were admitted during the year, 3 being inoperable and the 4th treated with radium.

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY OF THE UNIVERSITY OF HONG KONG. CLINICAL REPORT, 1940.

THIS report, which has been produced by Professor Gordon King, comprises the work done at the Tsan Yuk Hospital, and the maternity ward of the Queen Mary Hospital, the latter being under the care of the department for the first time.

During the year there were 4,373 deliveries with a mortality rate of 0.86 per cent. This high figure was accounted for by two factors, an increase in the number of eclampsia cases of a very severe type, and to beri-beri, which accounted, directly or indirectly, for 17 of the deaths.

This increased incidence of beri-beri was due to the state of overcrowding, malnutrition and distress among the lower classes from which most of the patients were drawn.

The antenatal clinics have grown in popularity, with the result that the number of booked cases admitted to the hospitals rose from less than 8 per cent in 1939 to 27.3 per cent in 1940: a very marked improvement.

Four hundred and four cases were admitted to the gynaecological department and 293 operations performed.

This is one of the best reports we have seen, well set out with an excellent series of tables including details of the gynaecological conditions and operations. May we express our sympathy with the University of Hong Kong in its present circumstances.

BRIANT EVANS.

BOOK REVIEW

"Obstetrics and Gynaecology in 1942." The 1942 Year Book of Obstetrics and Gynaecology. Obstetrics edited by JOSEPH B. DELEE, M.D.; Gynaecology edited by J. P. GREENHILL, B.S., M.D., F.A.S.S. (Pp. 704.) Chicago: The Year Book Publishers. London: H. K. Lewis. Price $3.00 or 16*s.* 6*d.*

THE annual appearance of the Year Book is most welcome, and Drs. DeLee and Greenhill are again to be congratulated on the excellency of their achievement. The abstracts are carefully chosen and remarkably lucid, and the comments of the Editors are most instructive and delightfully pungent.

This book should find a place in every gynaecologist's library, for does it not gather together in a compact and readable form an extensive literature which without this would be beyond his capacity to read and digest? Drs. DeLee and Greenhill do this for us and enable us to keep abreast of what is done across the Atlantic for it must be admitted that the greater part of the bibliography comes from the States—which is only natural and to be expected.

It is difficult to find adequate words with which to praise this little book and one looks forward with pleasant anticipation to the next.

D. M.

Review of Current Literature

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab.), F.R.C.S., F.R.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges.

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world; owing to the war many journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received. At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology, and Biochemistry.

LIST OF ABSTRACTORS

J. LYLE CAMERON, F.R.C.S.; W. E. CROWTHER, M.B.; R. H. B. ADAMSON, M.D.; B. JEAFFRESON, F.R.C.S.; P. MALPAS, F.R.C.S.; T. N. A. JEFFCOATE, F.R.C.S.; MEAVE KENNY, F.R.C.S.; JANE H. FILSHILL.

The Lancet

November 22nd, 1941.

*Placental blood in the treatment of amenorrhoea. J. Halbrecht.

November 29th, 1941.

High stillbirth and neonatal mortalities. Dugald Baird and John F. B. Wyper.

December 27th, 1941.

*Macrocytic anaemia in pregnant women on the Gold Coast. Beatrice Russell.

PLACENTAL BLOOD IN THE TREATMENT OF AMENORRHOEA.

The treatment of amenorrhoea and sterility with various gonadotropic hormones has been unsatisfactory in women and in monkeys up to now. Halbrecht suggests that gonadotropic preparations might fail because they contain an incomplete hormonal complex: they lack an activator which is present in the blood. This theory is partially confirmed by the positive results which have been recently reported from the use of serum of pregnant mares. Also because of this, the author decided to see the effect after using

placental blood. Placental blood suggested itself to him as it seemed to be rich in hormone which must be the causal factor in vaginal bleeding and lactation in the newborn. He administered 5 to 6 injections every other day of 150 to 200 c.c. of plasma or plasma and blood intravenously. The effect on the endometrium was controlled by curettage before and after treatment. He injected 34 amenorrhoeic women, with the result that 18 menstruated within 5 to 35 days and a further three menstruated on or after the thirty-fifth day. Of 11 patients showing atrophy of the endometrium before treatment, 6 had a normal endometrium after the course of treatment. The author is of the opinion that the action of placental blood does not depend on its folliculin content but on gonadotropic substances present in it. This was borne out by a patient who failed to menstruate after having had her second ovary removed two years previously.

MACROCYTIC ANAEMIA IN PREGNANT WOMEN ON THE GOLD COAST.

In this paper Beatrice Russell analyses 100 cases of this form of anaemia occurring in the Maternity Hospital from 1928 to 1938. They constituted about 1 per cent of the total in-patients, but she says that this figure does not represent the full incidence as only severe and definite cases come for admission. The author reports that it is difficult to detect anaemia among the dark-skinned by inspection alone, and slight cases tend to escape notice. Some cases develop very rapidly and in one case reported the haemoglobin dropped from 55 per cent to 38 per cent in six days while the red cell count fell to 1,360,000 per c.c. Multiparity was not found to be an important factor but the association of concurrent infections, especially malaria, did seem to play some part in the aetiology. The chief complaints were breathlessness, palpitation, weakness or giddiness; all of which denoted a severe degree of anaemia. Oedema was noted in 38 of the cases and often a slight blurring of the features, due to oedema of the face, was the chief sign of the trouble. The blood picture resembled that seen in true pernicious anaemia, decrease of the number of red cells, high colour index and the presence of megaloblasts; but poikilocytosis and anisocytosis were rare.

Without treatment the condition tended to progress rapidly; however, many cases tended to be cut short by the onset of premature labour. The woman might die during labour, or in the first day or two of the puerperium, but, if she survived this period, recovery often set in. The patient was considered to be in a critical condition if the haemoglobin was below 20 per cent, but even then the response to treatment was usually rapid and gratifying. If the patient was untreated, the outlook was bad unless labour was early. The prognosis was good under treatment, provided the patient was not *in extremis*, when first seen, and if she was not already in labour. In the puerperium low-grade sepsis made the treatment less satisfactory, and some of these cases tended to become aplastic in type.

Treatment was by rest in bed, full diet and raw liver, or liver extract by mouth, or by injection. If the patient would take it, half a pound of raw liver was given daily. Campolon was used in all severe cases from the middle

of 1935, 4 c.c. daily was needed to get a satisfactory result. Iron therapy was usually started as soon as the initial response to liver therapy was well established. Blood-transfusion was seldom necessary. Induction of labour was seldom required. Because of the prompt response to liver therapy, the author is of the opinion that macrocytic anaemia is not a disease of pregnancy but a disease associated with pregnancy.

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The British Medical Journal

December 6th, 1941.

*A case of combined intra-uterine and extra-uterine pregnancy. R. B. Leech.
Acquired immunity to blood-transfusion reactions; a new phenomenon. J. J. Wolfe and C. E. Das Gupta.
Hermaphroditism: a history approach. Report of Vicary Lecture by Dr. A. P. Cawadias.

January 10th, 1942.

*17-ketosteroid excretion in adrenal virilism. Jocelyn Patterson and Isobel M. McPhee.
Chemistry of oestrogens. Editorial.

January 17th, 1942.

*Ruptured aneurysm of the splenic artery during pregnancy. J. F. E. Gillam.
*Radiographs as a diagnostic aid in tubal gestation. S. Galewski.

January 24th, 1942.

*Observations upon breech delivery. L. G. Higgins.

January 31st, 1942.

*Acute appendicitis associated with intraperitoneal haemorrhage from rupture of the corpus luteum. Frank O'Gorman.

A CASE OF COMBINED INTRA-UTERINE AND EXTRA-UTERINE PREGNANCY.

The patient, aged 30, had had three children and was first seen at the fourth month of pregnancy when she was still menstruating slightly. When examined near term, two firm swellings were palpable and a provisional diagnosis of fibroid complicating pregnancy was made. On March 5th, 1941, a child, weighing 5½ pounds, was born after a normal labour. The patient had some abdominal pain two days after delivery, and there was no lactation. She was discharged home; but was readmitted on March 27th because the abdominal pain was more severe. The abdominal tumour was still present and foetal heart sounds were audible. At laparotomy the following day a child, weighing 6 pounds, was delivered from the abdominal cavity. It appeared normal, but lived for only half an hour. The placenta was attached by a pedicle to the right broad ligament in the position of the ovary. There was no connexion to the Fallopian tube. The placenta was removed and the patient made a good recovery.

The author comments that the absence of lactation may have been due to the patient's poor general condition, or to the inhibiting action of the extra-uterine pregnancy.

17-KETOSTEROID EXCRETION IN ADRENAL VIRILISM.

The 17-ketosteroids in the urine were estimated colorimetrically by a method which does not distinguish between androgens and inactive ketosteroids. The results, however, give an accurate indication of adrenal activity.

In normal women the ketosteroid excretion varies from 3.5 mgm. to 14.6 mgm. daily, with an average of 7.4 mgm., and bears no relation to the menstrual cycle. In normal men the amount varies from 9.4 mgm. to 20.9 mgm., with an average of 13.3 mgm. In babies and children the figure is extremely low.

In 4 cases of adrenal tumour, the excretion of ketosteroids was considerably more than normal, the highest amount being 270 mgm. in a woman. Except in cases of children, an excretion of at least 70 mgm. is necessary to establish the diagnosis, but a smaller figure does not exclude adrenal tumour.

Seven cases of pre-pubertal virilism were also studied. The results varied from 34 to 64 mgm. of ketosteroid. These figures are very high when compared with the normal for children. In young subjects the amount excreted may be so high as to make it impossible to distinguish between cortical hyperplasia and tumour formation.

In 67 cases of secondary, or post-pubertal, virilism variable results were obtained, the highest excretion figure being 33.4 mgm. Rather less than 50 per cent exhibited a higher figure than is normal for an adult woman. Many of these cases, however, had minor evidence of virilism, and may not have had any adrenal disease.

Cases of Achard-Thiers syndrome, hypogonadism, feminism in males, Simmond's disease and homosexuality in females, were also examined.

In general the level of ketosteroid output mounts in the following order: normal woman, normal man, secondary virilism, primary virilism, adrenal tumour. In some cases of secondary virilism the ketosteroid-creatinine ratio is raised even though the output of ketosteroid is within normal limits; this is of significance in the diagnosis of cortical hyperplasia.

RUPTURED ANEURYSM OF THE SPLENIC ARTERY DURING PREGNANCY.

Aneurysm of the splenic artery is said to be found in one of every 1,500 autopsies. Rupture of such an aneurysm was recorded 84 times up to 1939. Of these there were 27 intraperitoneal ruptures and 6 of the patients were pregnant at the time.

In this case the patient was a primigravida, aged 26. She was admitted to hospital at the eighth month with acute abdominal pain and collapse. A diagnosis of concealed antepartum haemorrhage was made and the foetal heart was inaudible. A dead child was delivered normally following artificial rupture of the membranes. The patient remained ill after delivery, and was treated as a case of acute dilatation of the stomach, being discharged

home on the fourteenth day. She was readmitted the following day with acute epigastric pain and collapse. After intravenous saline medication, the diagnosis was made by laparotomy and splenectomy performed. The aneurysm was not seen. The patient ultimately recovered.

Recorded cases indicate that the initial haemorrhage is frequently into the lesser peritoneal sac and is not fatal. It is the second haemorrhage about two weeks later which is so often fatal. The appropriate treatment is splenectomy.

RADIOGRAPHS AS A DIAGNOSTIC AID IN TUBAL GESTATION.

A case is described in which the diagnosis of unruptured tubal gestation was made by uterosalpingography, exploratory puncture of the pouch of Douglas having been without value as an aid to diagnosis.

OBSERVATIONS UPON BREECH DELIVERY.

A series of 84 uncomplicated breech deliveries is described. All the babies weighed 5 pounds or over, and 6 were stillborn.

Impaction of the breech is more likely to occur if the child is large, and induction of labour at thirty-seventh or thirty-eighth week is, therefore, advised. Providing the breech is low, artificial rupture of the membranes is the method advocated. Impaction due to contracted pelvis is rare.

If the breech does not engage, Caesarean section is the best treatment. When the breech becomes impacted at the vulva, extended legs should be brought down and delivery effected without undue delay. The ideal, however, is not to interfere in any way. Episiotomy is helpful.

The commonest cause of difficulty in delivery of the after-coming head is incomplete dilatation of the cervix. Extension of the foetal legs is, therefore, an advantage since it ensures better dilatation of the cervix. If the head is delayed at the brim, engagement should be assisted by allowing the foetal body to hang from the vulva, and by pressure on the head from above. If the head is delayed in the pelvic cavity, episiotomy and delivery by forceps is indicated. If necessary an air-way to the foetal mouth can be maintained by inserting a speculum into the vagina and the child may breathe before its head is delivered.

ACUTE APPENDICITIS ASSOCIATED WITH INTRAPERITONEAL HAEMORRHAGE FROM RUPTURE OF THE CORPUS LUTEUM.

The patient, aged 31 and nulliparous, was admitted two days after the onset of the symptoms and signs of appendicitis. At operation 26 days after the last menstrual period, free blood was present in the peritoneal cavity, and there was a pelvic haematocele with oozing from the corpus luteum in the right ovary. The acutely inflamed appendix was pelvic in position. The appendix was removed and the corpus luteum sutured. The cause of haemorrhage from a corpus luteum is unknown, but in this case it is suggested that abnormal hyperaemia of the right ovary due to the low-lying inflamed appendix may have been a factor.

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*Toxaemic pregnancy in relation to subsequent pregnancies, with special reference to renal function tests. V. I. Krieger and R. McK. Rome.

TOXAEMIC PREGNANCY IN RELATION TO SUBSEQUENT PREGNANCIES, WITH SPECIAL REFERENCE TO RENAL FUNCTION TESTS.

Krieger and Rome from the Department of Pathology, Women's Hospital, Melbourne, have analysed the histories of 652 patients whose renal efficiency had been determined by chemical tests during an initial toxaemia and who had had at least one subsequent pregnancy at the hospital during the last 10 years.

The patients were divided into the following groups: (1) those suffering from albuminuria A, in whom albumin was present in the urine for one day only; (2) B, in whom albuminuria was observed from 2 to 4 days; (3) C, cases of albuminuria of longer than 4 days' duration with, in addition, raised blood-pressure and oedema; (4) those suffering from pre-eclampsia as shown by raised blood-pressure, albuminuria and oedema with, in addition, any two of the following symptoms, headache, eye signs, blurring of vision, vomiting or epigastric pain; (5) those suffering from chronic nephritis, when there was evidence of permanent renal damage; (6) eclampsia, including only patients who had had typical eclamptic fits; (7) patients with accidental haemorrhage of the severe non-traumatic type; (8) patients with severe pyelitis, with symptoms persisting for some time and in whom it was suspected that inflammatory trouble had spread into the parenchymatous tissue.

Group (1) included 29 patients and of these 19 had normal subsequent pregnancies and 2 severe toxaemia. In these cases, because of the transient albuminuria, few function tests were made during the antenatal period. During the puerperium 21 cases were investigated; renal inefficiency was proved in the 2 cases in which a subsequent severe toxaemia of pregnancy occurred. Group (2) had 59 patients and of these 50 per cent had normal pregnancies following the toxaemic pregnancy. One-third of these patients had a second toxaemic pregnancy, mild in 7 and severe in 11. In these recurrent cases 4 out of 14 urea concentration tests conducted before delivery and 6 out of 11 made in the puerperium gave evidence of renal damage.

Group (3) included 171 patients and of these 60 showed toxaemic changes in succeeding pregnancies. Of these 60 recurrent toxaemic cases only 11 had albuminuria lasting for 4 days in the first pregnancy. The urea concentration test indicated renal inefficiency in 64 (71 per cent) of the 110 patients tested ante-partum. Only 33 (27 per cent) of 121 patients tested during the puerperium showed poor results 8 days after delivery. Group (4) included 74 cases, and of these there were 26 normal second pregnancies, 10 mildly toxaemic and 27 severely toxaemic as well as 11 abortions. In this group renal inefficiency was found in 31 out of 37 cases investigated before delivery and in 22 out of 49 cases tested after delivery.

The writers record that 355 eclamptic patients were treated during the

years 1930 to 1939 inclusive and that of these 51 died. The histories of only 106 came within the scope of their investigation. Normal pregnancy followed in 43 cases, and of the 13 who had still further pregnancies 3 showed toxaemia in still further pregnancies. One of these three was toxaemic in a fourth pregnancy.

Many eclamptic patients were too ill to have renal function tests carried out before delivery; 9 out of 18 tests performed gave indication of severe renal damage; 20 out of the 59 urea concentration tests gave abnormal results in the puerperium. In subsequent pregnancies 14 of the 50 tests made post-partum showed renal inefficiency. In this group many of the subsequent toxaemias were of the pre-eclamptic, eclamptic or chronic nephritic variety.

Group (7) had 25 patients whose initial pregnancy was complicated by accidental haemorrhage. Of these 6 had a subsequent normal pregnancy, 2 had mild toxaemia and 17 had a severe toxaemia. Only 5 of these patients had a second subsequent pregnancy.

Group (8) comprised 48 cases of severe pyelitis. Of these 22 had a subsequent normal pregnancy, 8 aborted and 18 had a toxaemic pregnancy; 11 of the toxaemic cases had further pyelitis. One patient in this group had accidental haemorrhage and one had eclampsia.

In the chronic nephritic group 66 patients were eventually classified; 11 were so diagnosed in the initial toxaemia and 55 in later pregnancies. There were relatively few subsequent pregnancies after the diagnosis of chronic nephritis was made, namely, 14 pregnancies in the 66 cases investigated.

Renal function investigation showed the presence of gross renal damage in 25 per cent of the 56 cases investigated ante-partum. Six cases out of 17 tested post-partum were abnormal. Urea concentration tests showed 70 per cent to be abnormal out of the 43 investigated.

The initial toxaemia of pregnancy occurred chiefly in patients aged under 30 years. This would be expected as 63 per cent of the patients were primigravidae.

The investigation gave no information as to the number of patients who were toxaemic with their first pregnancy and who did not again become pregnant. During the present investigation it was found that 60 per cent of the patients had no further pregnancy even when the second pregnancy ended normally or in an abortion. The incidence of further toxaemic pregnancy was particularly marked after severe initial toxaemia and of all the varieties the greatest risk followed severe accidental haemorrhage.

The incidence of chronic nephritis appeared to be most marked after Group (3), in actual numbers, but worked out on a percentage basis the proportion in each group did not show any significant variation.

It was found that after a toxaemic pregnancy 15 per cent to 20 per cent of the following pregnancies ended in abortion. After mildly toxaemic pregnancy more than half the subsequent pregnancies ended normally; when toxaemic changes did occur they were usually of the variety in Group (3). No case of eclampsia or pre-eclampsia followed Group (1) in this series. After severe manifestations only 35 per cent to 40 per cent were followed by normal pregnancies.

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